USING EXERCISE TO TREAT DEPRESSION: AN ANALYSIS OF CLINICAL AND SOCIAL PERSPECTIVES

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ABSTRACT

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Title: Using Exercise to Treat Depression: An Analysis of Clinical and Social Perspectives

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Mental health issues are often difficult to treat, not only because many individuals do not have the money or access to seek adequate treatment, but also because the stigma associated with these illnesses often stops people from seeking help. I propose that exercise is a promising solution that can help individuals overcome both of these obstacles. The goal of this thesis is to analyze the relationship between depression and exercise, in order to understand the mechanisms through which it exerts its positive effects, and how best to treat patients with depression. It also acts as a guide to setting up preventive measures for the general public at large.

This thesis starts by taking a look at the illness known as depression, including its history, cultural significance, pathology, and treatment options. It then moves to understanding exercise, including how exercise affects healthy individuals neurologically, as well as the evidence that shows its effectiveness in reducing depressive symptoms in patients. Finally, it suggests various routes of action to help therapists and patients utilize exercise to treat cases of depression, especially as a supplement to existing methods of treatment; and various public health interventions that communities and policy-makers can use to improve the health of the public.

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INTRODUCTION

As the conversation around mental health is becoming louder around colleges across the nation, I decided that this was an apt topic to choose for my senior thesis. I was motivated in part through my own experience dealing with depression as a sophomore in college, and my success in recovering after utilizing much healthier habits to take care of myself, namely through exercising, as well as altering my diet and sleep pattern. Because the changes I made for myself had such a positive impact on my health, I decided to focus on them in my thesis. I hope that this work can both convince others to prioritize exercising as a necessary habit, and also provide an explanation into why it works so well. Although this avenue is not the only one we can use to treat depression, this is one of the methods that perhaps individuals have the most control over, and may prove to be the simplest to implement.

This brings me to the other reason motivating me to write this thesis: mental health issues are facing quite a few barriers that can limit our treatment options. For one, access to healthcare is very limited for many populations suffering from mental health issues, as they tend to be lower income populations who have historically been discriminated against. Not only this, but those who do have access often find it difficult to recover simply because of the length of time, money, and effort that is required from them in order to see change. Finally, the stigma associated with mental health issues, which can paint them as weaknesses, often stops many people from seeking help.

I believe that the best way to tackle these issues is by giving individuals more control over their own lives and helping them change their habits, so as to empower them and place them in a position to speak about their issues more freely. The phrase "I'm seeing a therapist and taking medication because I've been feeling down recently" sparks a vastly different connotation than the phrase "I've been going to the gym to exercise more frequently because I've been feeling down recently." More than this, it puts these individuals in the driver's seat as an active participant in their recovery, as opposed to a passive spectator. This is why I believe that it's extremely important to explore exercise as an option to treat mental health issues, and help promote discourse and further research into this crucial field.

In my thesis, I'd like to start by taking a look at the illness known as depression, including its history, cultural significance, pathology, and treatment options. I will then explain how exercise affects healthy individuals neurologically, as well as the evidence that shows its effectiveness in reducing depressive symptoms in patients. Finally, I will suggest various routes of action to help therapists and patients utilize exercise to treat cases of depression, especially as a supplement to existing methods of treatment; and various public health interventions that communities and policy-makers can use to improve the health of the public.

CHAPTER 1: DEPRESSION

The History of Depression

Previously known as melancholia, depression has long been studied by physicians and philosophers alike. Historians generally believe that the ancient Mesopotamians were the first people to account for this ailment, in the second millennium, BC.[1] They, and many subsequent cultures, hypothesized that the symptoms of melancholia were caused by evil spirits and black magic, and attempted to treat their patients by using religious interventions like starvation or beatings to drive out supernatural forces. These interventions, tended to by priests, were the products of a more spiritual attitude towards depression, which was also reflected in subsequent cultures like the Ancient Chinese and Ancient Egyptians.[2]

The Ancient Greeks, however, used a more biological approach to this ailment. Hippocrates, who based his understanding of the body and its diseases on the four humors, believed that melancholia was caused by an overabundance of black bile.[3] He believed that the proper way to treat this ailment was through methods such as bloodletting and taking baths. As time went on, the two aforementioned theories experienced periods of cyclical dominance and regression. Roman scholars such as Galen and Persian physicians like Rhazes believed that mental illnesses were biological in nature, and promoted treatments that revolved around taking baths, proper nutrition, and even rewarding individuals for behaving in a positive manner.[4, 5] However, theories shifted back towards their religious roots during the Middle Ages, and priests and religious figures once again emerged to seek out methods like exorcisms or imprisonment.

After the Renaissance, the conversation around depression began to change again. Robert Burton's *Anatomy of Melancholy,* published in 1621, took an in depth look into this issue, and expanded the discussion to include social issues such as loneliness and poverty.[6] He was one of the first scholars to recommend relying on a combination of more modern treatments such as diet, sleep, and social support to help treat this issue. Largely due to his efforts, physicians started to create a more focused view of melancholia, and attempted to define it more clearly. Previously, melancholia had been attached to a broad range of symptoms, from sadness to fear, and anger to insanity. Francois de Sauvages divided the term melancholia into 14 "species," distinguishing between ailments like "ordinary melancholia," "religious melancholia," and even "hippanthropic melancholia," the fear of being transformed into a horse.[7] Other physicians began to add to the growing body of work, and the term "mental depression" was first used in this context by Emil Kraepelin in 1883 in the 1st edition of his *Textbook.* This would become one of the most influential works in the budding field of psychology, and would earn Kraepelin the title "The Founder of Modern Scientific Psychiatry."[8] He was also one of the first to argue for a distinction between endogenous depression, which he believed had a more biological basis, and exogenous depression, which was said to be caused by external factors such as stress.

Freud, who was at the time developing his theories on psychoanalysis, contextualized these ideas under unconscious processes that had deep roots in his patients' childhood experiences.[9] He also helped distinguish the diagnosis of classical depression from the feelings felt by those in mourning, emphasizing that psychoanalysis was required to treat the former, which had deeper psychological roots than the latter. Adolf Meyer expanded on this idea by arguing that in most cases, it was how patients reacted to their conditions that mattered, and that treatment should focus on prevention for the future, ultimately culminating in his proposal to forgo the term melancholia for the more specific word "depression."[10]

In 1952, the first edition of the Diagnostic and Statistical Manual of Mental Disorders, or DSM-I, was released, which helped standardize the diagnosis and treatment of depression and many other psychological disorders.[11] While it initially characterized the disorder as a "depressive reaction," the manual's categorization of depression has evolved over time, and the DSM-V, released in 2013, now categorizes many similar but distinct ailments under the category "depressive disorders," differentiating between major depressive disorder, persistent depressive disorder or dysthymia, substance-induced depressive disorder, and many other diagnoses.

It is important to note that the DSM-V is a product of the continually changing psychological landscape, and future editions may be quite different from what we are seeing today. Much of the debate in this field lies around the classification of depression under a unitary or binary model, which have experienced a sort of tug-of-war over the past half-century. Binary models, which were more popular in the early 20th century, argued for a more complete analysis of patients' symptoms, using their past experiences in conjunction with their present personal and socioeconomic profile to arrive at an effective solution.[12] Freudian psychoanalysis, Beck's cognitive triad theories, and humanism, which focused on self-actualization and the search for meaning in life, were some of the philosophies that pushed for this view on depression and psychological illnesses. Critics of these theories, however, argued that these ideas had no biological basis, and that depression was an illness that needed to be analyzed neurologically and treated as a medical condition.[13] Unitary models, which framed depression under the severity of patients' symptoms, started to become more popular towards the late 20th century, spurred on by new research into neurotransmitters and theories of neurochemical imbalances, as well as the use of rapidly advancing medical technology and structural imaging.[14]

More recently, binary models have started to grow in popularity again, as researchers are finding that some patients do not react to medication alone, and require a combination of medication and therapy to see the best results. Some of the attitudes surrounding this shift included the criticism that under unitary models, the diagnosis of depression was essentially turned into a checklist, one that did not place enough importance on clinically distinguishing between the causes of these symptoms.[15] Therefore, it is critically important that the reader understand that although much of this thesis focuses on the impact of exercise in the framework of the unitary model, individuals suffering from depression are encouraged to work with mental health professionals to determine if there are endogenous and exogenous causes to their mental health issues, so that they can receive the most complete care possible. As we will see later in this paper, most data has revealed that patients who display the greatest improvement are those who successfully combine exercise with other forms of treatment, like therapy or medication.

Depressive Disorders at a Glance

Let us now focus on depression as an illness, and differentiate between general sadness and clinical depression. Feelings of sadness or discontent are relatively common among populations, but generally temporary, and are most often reactions to acute events and stressors in someone's life. Even the most severe symptom of sadness, crying, is normal from time to time. A 2002 study found that on average, American men cried about twice a month, and American women cried about three and a half times per month.[16] However, what distinguishes depression from general sadness is the fact that depressive symptoms tend to be much more severe and last much longer, and include symptoms such as a significantly lowered mood, irritability, and anhedonia or a loss of interest in activities that one normally enjoyed. If these

symptoms last at least two weeks, they can be classified as a depressive episode, which actually usually lasts for about 6 months, on average. If these episodes are recurrent, the patient is diagnosed with major depressive disorder.[17]

According to the DSM-V, Major Depressive Disorder, or MDD, is characterized by the presence of at least five of the following symptoms during a two-week period, with at least one of the symptoms being either a depressed mood, or a loss of interest or pleasure, or anhedonia:[18]

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (Note: In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

Most of these symptoms are not universal, and often differ by gender and age. For example, men tend to experience physical pain, such as headaches, as well as greater irritability, suspicion, and anger, and display more impulsive behavior. Women are more likely to experience emotions like guilt and shame, are more likely to be anxious, and display passive behaviors in an attempt to avoid conflict.[19] When age is taken into account, older adults tend to display symptoms of atypical depression, which often manifest as somatic, physical symptoms. They also tend to suffer more from anxiety than their younger counterparts, and psychotic symptoms are often common in this subpopulation as well.[20] There are also a few different manifestations of depressive symptoms in disorders that are similar to major depressive disorder, but differ in their prognosis, duration, or etiology:

Persistent Depressive Disorder, or dysthymia, is akin to a "milder" form of depression, and affects about 1.5% of adults over the age of 18 in the US.[21] This is primarily characterized by anhedonia, and involves the individual experiencing a slightly lowered mood, and a flattened affect over at least a year, a much longer period of time than is needed to diagnose MDD.[22]

Atypical Depression is most often diagnosed in individuals who may not display the same symptoms that individuals with MDD display. Some of these symptoms can include irritability, oversleeping, overeating, and most commonly, a general sense of heaviness, as patients can claim that their limbs are dragging them down.[23]

Seasonal Affective Disorder, or SAD, is a form of depression that is related to the amount of sunlight that individuals receive. Those with SAD tend to display lowered moods in the winter, or if they live in parts of the country that receive less sunlight, as evidenced by its 1.4%

prevalence in Florida and its 9.9% prevalence in Alaska.[24] This may disrupt patients' melatonin and serotonin levels, and subsequently, their circadian rhythm. This form of depression is often easily treated with phototherapy (light therapy). By providing them with greater exposure to light, we can promote greater activity in their serotonergic neurons, limit serotonin transporter activity, and greatly improve their mood.[25]

Psychotic Depression is a rare form of depression that occurs when severe depressive episodes cause hallucinations or delusions that are commonly seen in schizoaffective disorders. The psychotic symptoms often develop after the patient has experienced a previous depressive episode, but can last longer than the initial depressive episodes. These patients tend to show the greatest responsiveness to secondary treatments like electroconvulsive therapy, or ECT, and transcranial magnetic stimulation, or TMS.[26]

Postpartum Depression affects women who have just given birth. Although most new mothers experience mood swings and acute feelings of sadness known as the "baby blues," these are usually temporary and do not last longer than a few weeks. However, about 15% of women experience chronic symptoms that can affect their appetite and mood, and can hinder their ability to care for their child.[27]

Disorders that are related to depression include bipolar disorder and anxiety disorder. Bipolar Disorder, also known as manic-depressive disorder, involves alternating episodes of mania and depression over long periods of time. Individuals experiencing a manic episode often have a high level of energy, speak quickly, display increased irritability, and experience difficulty concentrating.[28] Present in about 2.6% of the population, bipolar disorder is most commonly treated with lithium, which primarily acts as a mood stabilizer and flattens manic episodes while alleviating depressive symptoms. It also seems to be the most effective at reducing the risk of suicide among patients, out of other treatment options.[29] The term "anxiety disorder" encompasses a broad number of related disorders; however, they are all classified by feelings of severe anxiety and fear, even when there is no present danger. Because anxiety disorders are closely related to depressive disorders, we will mention them later in this thesis, as it has been found that resistance training may prove to be beneficial towards patients suffering from anxiety.[30]

There is growing evidence that depression has a genetic basis, as it and other mood disorders seem to run in families. In fact, first-degree relatives of individuals with depression are more than twice as likely to have depression as unrelated individuals.[31] On top of this, probands who suffer from more severe depression, experienced more recurrent episodes, or had an earlier age of onset, tended to have relatives with higher rates of depression.[32] Twin studies conducted in this area have also shed light onto this topic. Research has found that when one twin is affected by major depressive disorder, the chances of his or her twin also having MDD is more than two times greater if the twins were monozygotic, rather than dizygotic.[33] If the first twin has MDD, their monozygotic sibling has an almost 50% chance of also developing MDD, while a dizygotic sibling has a 20% chance. When researchers probed further for other mood disorders, they found an even stronger 67% correlation for bipolar disorder between monozygotic twins, as compared to a 19% correlation between dizygotic twins.[34]

There are also differences in the manifestation of major depressive disorder with respect to men and women. Meta-analysis of the genetic basis of MDD have found a heritability of 42%, on average, for women, and a heritability of 29%, on average, for men.[35] Explanations for these

sex differences have tried to focus on the sex chromosomes, as well as the differences between the concentrations of male and female sex hormones, but much of this research is still in its developmental stages. Researchers are still struggling to pinpoint specific genes that control for depressive disorders. One of the genes that is being looked at is 5-HTTLPR, which codes for the serotonin transporter protein, but most studies have found no significant relationship between variations in this gene and cases of depression.[36, 37] One gene that has shown promise is the gene coding for the brain derived neurotrophic factor protein, or BDNF, which we will discuss later in this paper.[38]

Current Statistics

Depression is the leading cause of disability in the world today. About 300 million people worldwide have experienced a depressive episode at some point in their lives, according to the World Health Organization.[39] And according to the National Institute for Mental Health, as of 2017, about 17.3 million adults in the US have experienced at least one major depressive episode in the past year, which amounts to 7.1% of the US population.[40] A higher percent of women fell under this category, at around 8.7%, as compared to only 5.3% of men. Interestingly, this percentage increased among those who reported themselves to be biracial or multiracial, at a prevalence of about 11.3%. Indeed, many bi- or multi-racial individuals often report higher rates of social isolation due to their inability to identify fully with a single cultural group, and individuals who believe they do not have a stable racial identity have lower self-esteem than their peers.[41] The median age of onset is during the early 30's for most individuals; however, the demographic with the highest rate of depression is young adults between the ages of 18 to 25, with about 13.1% of them reporting that they have experienced a major depressive episode at least once. When we consider the fact that these individuals must make sense of the financial, vocational, scholastic, and social pressure that is placed on them, it is understandable that this population is the most vulnerable to this disease.

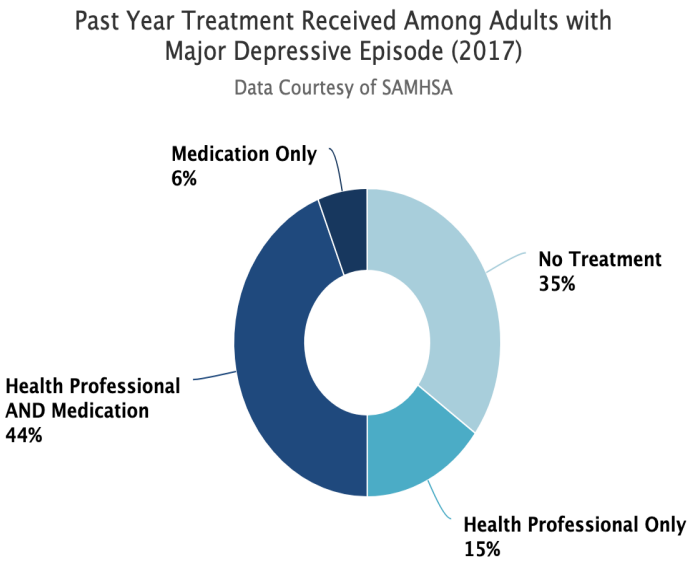
Although it is common to believe that depression is only a disease that affects the mind, it is also associated with many physical comorbidities. Of the adults who have experienced depression, almost two thirds of them also reported having a concurrent physical or mental impairment. According to previous surveys conducted by the NIMH, 25% of cancer patients, 10-27% of stroke survivors, almost 33% of those living with HIV, and 50% of those affected by Parkinson's disease suffer from depressive episodes. Individuals with depression are also four times as likely to develop a heart attack as those who have never experienced the disorder.[42] In women, researchers have found that the hip bone density in women who experienced multiple depressive episodes was about 10-15% lower than women who had no history of the disease, which amounted to a 40% increase in the risk of hip fracture over a decade.[43] Among those suffering from mental health issues, a majority of patients with eating disorders and almost a third of those with substance abuse disorders have experienced depression as well. On top of this, about half of all individuals diagnosed with depression are diagnosed with an anxiety disorder as well.[44]

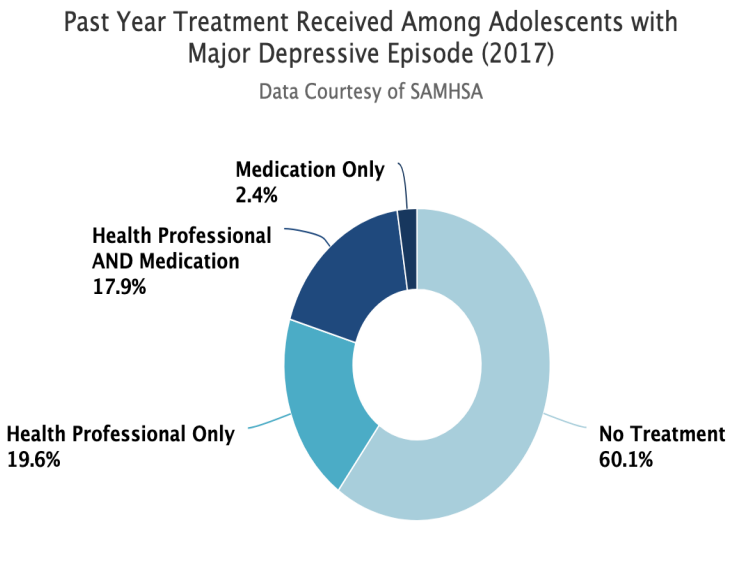
The impact of depression on Americans cannot be understated. It is the leading cause of disability in the US for people between the ages of 15 to 45.[45] Mood disorders like MDD and bipolar disorder are the third most common cause of hospitalization for this age group in the US.[46] Experts estimate that depression among US workers has cost the country more than $200 billion in medical billing and lost productivity, with lost workdays amounting to about $12

billion. An estimated $11 billion is lost solely to decreased productivity, as measured by problems caused by loss of energy and poor concentration and decision-making, although these numbers may be largely underestimated due to many Americans who are left undiagnosed, or who fail to report such issues.[47] On a larger scale, suicide has been on the rise in America, serving as the 10th leading cause of death in this country. Last year, 9.8 million adults experienced serious thoughts of committing suicide, and 1.3 million adults made an attempt on their own lives. Almost 45,000 Americans took their own lives in 2017, with more than 90% suffering from some mental health issues, and two-thirds suffering from depression.[48] This issue disproportionately affects older adults, who have a suicide rate more than 50% higher than the rest of the population – much of this is thought to be due to undiagnosed or untreated depression.[49] Among adolescents, the suicide rate for young men is almost 7 times that of the rate of young women. In developing countries, 75% of individuals with mental health issues do not receive proper treatment, and almost 1 million individuals take their own lives worldwide.[50]

The data on the treatment for depression also sheds some light on how we are dealing with these issues. Fortunately, the NIH reports that around 70% of those who have been treated for depression have shown a marked improvement in their symptoms after attending both therapy sessions and starting new medication.[51] Of the adults who did decide to seek treatment, the vast majority chose to do so through a combination of therapy and medication treatment. Researchers at the Depression and Bipolar Support Alliance have found that support groups were a strong predictor of compliance, with patients in peer groups being 86% more likely to continue taking medication and believe that their side effects were manageable.[52] The DBSA has found that for those who did not show improvement, almost half could be accounted for through noncompliance, including an inability to cope with their medication's side effects, fears of becoming addicted to their medication, as well as financial pressures that made them unable to seek continuous treatment.

Unfortunately, it has been estimated that these cases only account for a third of the true number of individuals suffering from depression in the US, as many factors, including stigma and financial struggles, may prevent others from seeking help. More than 35% of adults and a staggering 60.1% of teenagers did not receive any treatment for their experiences every year, as displayed by the graph below.[53] One of the reasons for this large number in children is that, unfortunately, the average delay between the onset of symptoms and intervention tends to be between eight to ten years, whereas for adults, it tends to be less than a year, on average.[54] Women are twice as likely to reach out for help as men, who often tend push aside troubling, yet less severe thoughts and feelings until they grow much more intense.[55]





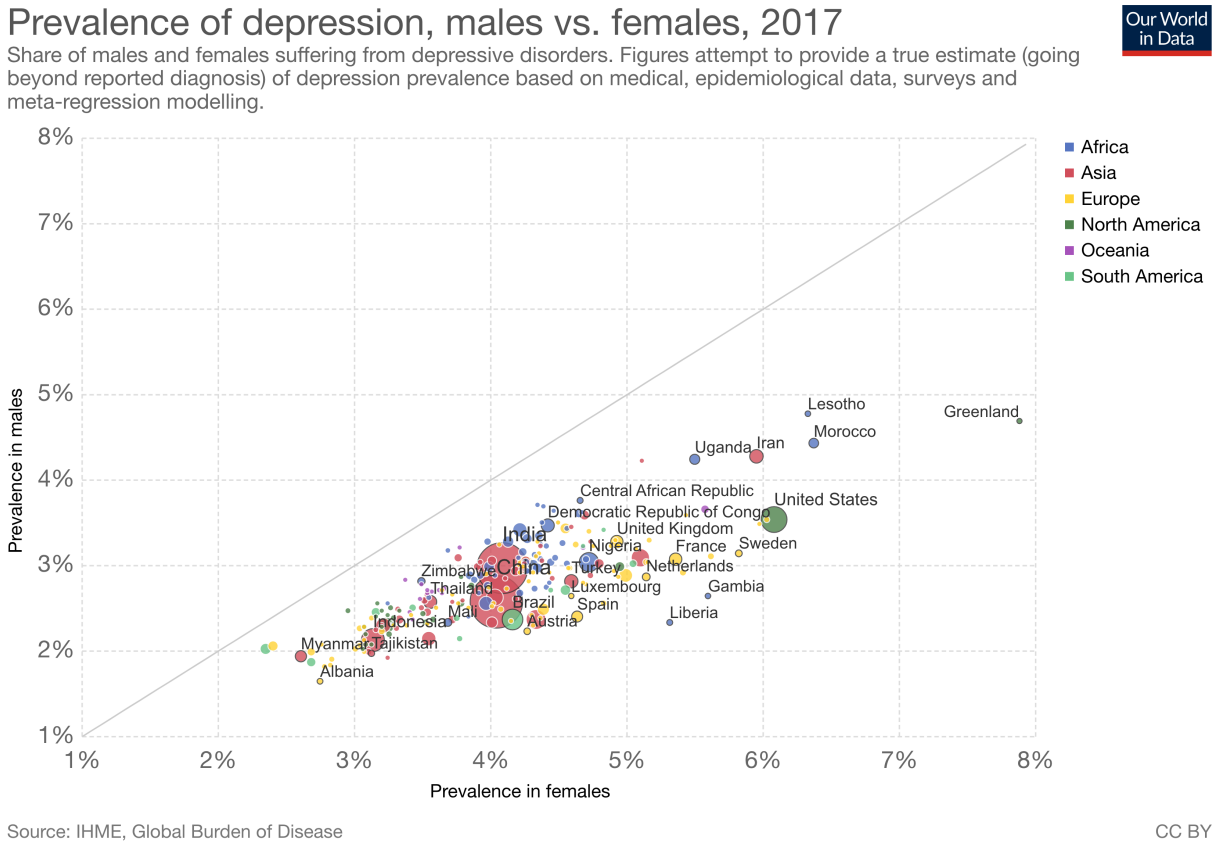
It is important to note that attitudes towards depression also can vary among different cultures. Western cultures' emphasis on individuality and eastern cultures' emphasis on collectivism both provide unique barriers to understanding those who are suffering from mental health issues.[56] For example, an individual in the west may feel that there is nobody around them they can confide in, and if they do find someone, they may refrain from opening up too much, under the assumption that they are a burden to their companion. In the east, this may manifest itself in the fear of speaking out due to a desire to fit into the group. By keeping their emotions bottled in, they may assuage common fears such as social anxiety, a deterioration of their reputation, a loss of privacy, or their concerns that they may disrupt group productivity. But this then may weaken their sense of individuality, and can cause them to stop prioritizing, or even neglect, their own health.

A meta-analysis conducted by York Hagmayer and Neele Engelmann analyzed the differences between western cultures and non-western cultures, and actually discovered that both cultures had similar ideas regarding the cause of depression.[57] Generally, most people from both cultures believed that environmental factors, such as familial or occupational stress, were the primary causes of depression, with psychological causes and individual personalities being second, and biological causes actually being third most important. However, the two cultures differed with respect to their preferred treatment options. Western cultures tended to rely on psychological therapy as their primary treatment method, with social support being a second option, and biomedical treatment being their third option. Nonwestern cultures ranked biomedical treatments as their preferred option, turning to social support as second, and opting for psychological therapy last. One of the reasons for this surprising difference in treatment may be due to the fact that psychological treatments are often not available, or not as well known outside of the west.

Many prevailing theories of depression were formulated in the Western world, and may have been focused on treating traditional Christian cultures that do not accurately represent the

modern heterogeneous world as it is today. These cultural differences may make it more difficult for psychologists and physicians in multicultural societies such as the US to treat minorities and people of color, who may in turn have more difficulty in trusting their mental health professionals. In fact, people of color tend to receive poorer healthcare than Caucasians in the United States. White Americans are almost twice as likely to use mental health services as African Americans, and Asian Americans are the social group least likely to use mental health services at all.[58] However, this may be due to the higher stigma among Asian populations about seeking out and receiving such treatment. Multi-racial individuals also experience their own unique set of problems that result in higher rates of depression, as mentioned earlier.

Mental health within the LGBTQ community is a rapidly growing issue as well, as researchers have found that LGBTQ individuals are twice as likely as straight individuals to suffer from depression. On top of this, LGBTQ youth are almost five times as likely to attempt suicide as straight youth are.[59] Researchers have also paid special attention to women, who experience depression at higher rates than men, perhaps due to the fact that they encounter more social, economic, and political problems than their male counterparts. A graph showing the prevalence of this disparity across the globe is attached below.[60] As we have already seen, post-partum depression is another factor that may contribute to these higher rates. However, black, white, and Hispanic women are almost twice as likely to use mental health services as men are.[61] This does raise questions about why depressed men are not seeking treatment, and whether the statistics on male depression are deflated, perhaps due to the increased stigma placed on men who acknowledge their emotions or choose to seek help.



Treatment Options

Conventional Methods

There are a number of methods currently being used to treat depression, including numerous methods of therapy and multiple classes of medications.

Therapy is the most commonly used method of treatment for depression, with cognitive behavioral therapy, or CBT, being the preferred route, as it has proven to be the most well researched and most effective for most patients.[62] The main goal of CBT is to empower its patients to challenge negative thoughts about themselves and promote positive thoughts in their place. By continually asking its patients to practice such skills, CBT allows patients to exert a greater sense of control over their recovery process, and eventually change their attitudes towards common scenarios. It generally takes about 3 to 4 months for patients to see the effects of their hard work. Studies have shown that CBT works just as well as medication in patients with moderate depression, and especially is successful in adolescents with moderate depression, although children with milder symptoms and better reasoning skills tend to see more success.[63] Importantly, CBT can allow individuals to quickly return to their commitments, as evidenced by a 2014 study conducted on nurses at a Singaporean hospital – allowing nurses to participate in regular CBT sessions allowed them to manage their stress so effectively that the hospital saw a reduction in the number of sick days that its participants requested from work each year.[64]

Interpersonal therapy is another form of therapy that is often used to help individuals through relationship-related issues. By providing a supportive group for these patients, usually comprised of their family members or other peers, therapists allow these individuals to share their experiences with each other, and learn how develop healthier interactions with others.[65] Interpersonal therapy lasts for about as long as CBT, and is especially helpful for older adults with depression, who tend to respond better to social support than individual sessions.[66]

Psychodynamic therapy, first developed by Freud, places emphasis on individuals' past experiences, and allows them to confront unconscious memories that may be the root cause of their current pain. Currently, the focus of this therapy has shifted from events in the distant past to more recent events in patients' lives, as well as additional social factors that may have influenced their mood.[67] This form of therapy is much more variant than the aforementioned techniques, and can last for years at a time, depending on how much of the patients' life and circumstances the therapist feels there is to unpack.

Recently, there has been a greater shift towards using medication to help treat depression, either by itself, or more commonly, in conjunction with therapy, a trend we will explore later in this thesis.[68] Among the medications currently being used, there are four major classes that tend to be most commonly prescribed:

Selective Serotonin Reuptake Inhibitors, or SSRI's, work by interfering with the serotonin transporter, SERT, which is used to reuptake serotonin into the presynaptic neuron after it is released. By increasing the levels of serotonin at the synapse, it allows more to remain there to bind to the postsynaptic receptor, thereby "artificially inflating" the patients' levels of this neurotransmitter.[69] Some examples are Prozac (fluoxetine), Zoloft (sertraline), and Paxil (paroxetine). This class tends to display the most consistent results between its various constituents. SSRI's tend to be the first, and most common medications prescribed, due to their

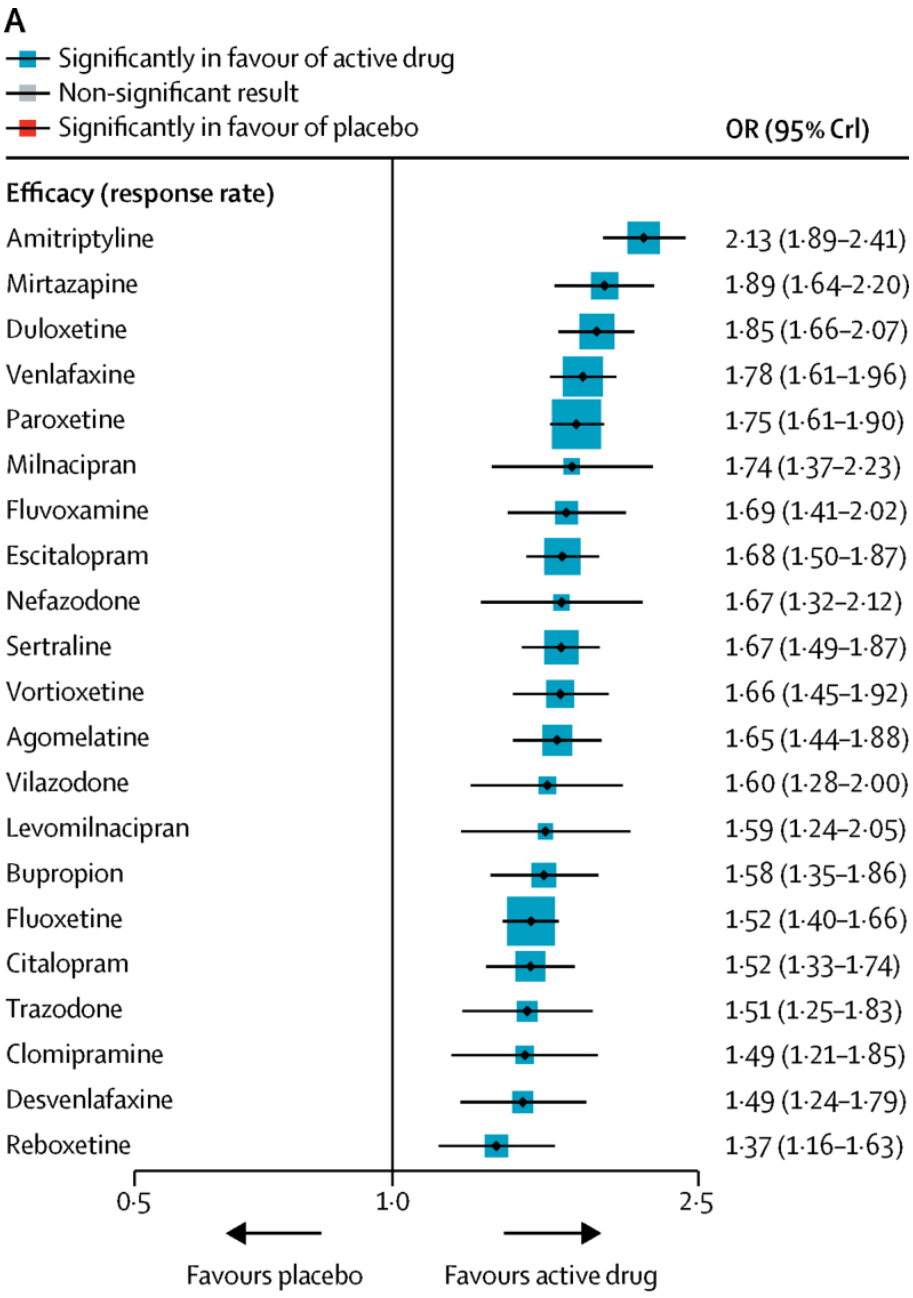
minimal side effects, and subsequently higher patient compliance rates. They are also the easiest to administer, as they only need to be taken once per day.[70]

Serotonin and Norepinephrine Reuptake Inhibitors, or SNRI's, exert their effects at both the serotonin and norepinephrine transporters. These were developed as a more balanced approach to altering patients' neurotransmitter levels, as a means to keep their monoamine levels in check.[71] The advantage of these medications is that by acting at multiple levels, they can treat a larger range of illnesses that span beyond mood disorders, and into the realm of Attention Deficit Hyperactivity Disorder, or ADHD, and Obsessive Compulsive Disorder, or OCD, as well as neurological conditions like fibromyalgia and neuropathic pain. Among the newer classes of antidepressants created, they tend to be as effective as SSRI's, and do not induce many of the side effects seen in previous classes.[72] The most commonly used SNRI's are Cymbalta (duloxetine) and Effexor (venlafaxine).

Tricyclic Antidepressants act through mechanisms similar to that of SNRI's, and block the reuptake of norepinephrine and serotonin from the synapse.[73] Some examples of TCA's are Elavil (amitriptyline), Trofranil (imipramine), and Norpramin (desipramine). TCA's were one of the first classes of antidepressants created, but have fallen out of favor due to the invention of the newer classes listed above, which came with fewer side effects.[74] This is also one of the reasons why they are currently classified under a different category as SNRI's. Currently, these tend to be used as a second-line of defense for patients with more severe depressive symptoms who have not responded to SSRI's or SNRI's, or patients who experience more somatic, physical symptoms. They should not be used for individuals with heart conditions or kidney and urinary problems, and can induce mania in some patients.[75]

Monoamine Oxidase Inhibitors target monoamine oxidase, a protein that breaks down intracellular serotonin, norepinephrine, and dopamine, preventing it from reducing their levels in the brain.[76] Much like TCA's, MAOI's were some of the first antidepressants developed in the 1950's during the birth of pharmacology, but are now only used as back-up medications, due to their many side-effects.[77] These also require adherence to a strict diet, as they can react dangerously with foods like cheeses and certain wines, as well as other medications, including birth control pills. However, these medications can be very effective for individuals suffering from atypical depression, who experience symptoms of fatigue and may struggle to handle interpersonal relationships.[78]

On the whole, most research strongly supports the efficacy of antidepressants. A 2014 study completed by the FDA, which analyzed all of the antidepressant trials it had received since 1985, found that on average, treatment with one or more antidepressants decreased depressive symptoms in about 50% more patients than those treated with a placebo.[79] These results were matched by national reviews in other countries, including Great Britain and Canada. The results of the British meta-analysis are shown below.[80, 81]



Antidepressants usually take a few weeks to start working, and treatment must be sustained for at least 4 months after remission to lower the chances of relapse, although a longer timeline is often recommended based on the patient's history.[82] It is important to note that according to most guidelines for treatment, antidepressants are not recommended for patients under 18, or those dealing with milder cases of depression, as generally researchers have found better prognosis for these individuals through therapy. Research has also found that there is a higher risk of suicidal behavior in younger patients who use SSRI's.[83] However, clinical trials

have found that Prozac (fluoxetine), an SSRI, is the only antidepressant to date that has proven to be effective in treating children.[84]

Electroconvulsive therapy, or ECT, and transcranial magnetic stimulation, or TMS, are also used in rare cases, when other treatments have proven to be ineffective. Although they may sound frightening, they are both FDA approved methods that can be relatively effective as the last lines of defense for cases of treatment resistant depression.[85]

ECT is a treatment in which surgeons induce small seizures in their patients' brains, either bilaterally or unilaterally, about two to three times per week until their symptoms subside.[86] ECT is still poorly understood, but it seems to exert temporary anticonvulsant effects on patients' frontal lobes by decreasing blood flow and metabolism in this region.[87] It also seems to support long-term neural plasticity and neurogenesis in the medial temporal lobe by increasing blood flow to these regions, and consequently improving their metabolism.[88] Although it is effective for about half of the individuals it is performed on, many of these individuals relapse within one year. Therefore, ECT is often accompanied by mediation, as well as follow-up ECT appointments.

TMS is a method that involves placing a strong magnetic field near the brain to induce an electrical current at that region. In depressed patients, the procedure often targets the left dorsolateral prefrontal cortex, which is responsible for executive functioning, including working memory and reasoning skills.[89] This is much less invasive than ECT, and seems to have relatively few side effects as well.[90]

Lifestyle Management

Other, less invasive methods also include lifestyle management, which is often done primarily through regulating patients' nutrition and sleep patterns, as well as in tailoring exercise routines.

In analyzing patients' sleep patterns, scientists have found that most individuals who are depressed cycle through their initial sleep stages quickly and spend more time in REM sleep.[91] To explain these findings, these studies have suggested that REM sleep is brought on due to decreased levels of serotonin, specifically in the brain stem.[92] In fact, antidepressants that increase serotonin levels in these areas have been known to hinder the onset of REM sleep.[93] Strangely, one study has found that actually asking individuals to pull an all-nighter increases activity in serotonergic neurons, and promotes improved moods among patients. However, prolonging this period of sleep deprivation had far worse consequences, as their mood dropped to even lower levels than it had been before they had started their deprivation period.[94] This implies that this increase in serotonin may be a temporary compensatory mechanism, rather than directly therapeutic in nature.

The role of sleep in depression must be further analyzed, as the data around it seems to be almost paradoxical – individuals who receive too little sleep are susceptible to depression, but the same can be said for those who spend too much time sleeping.[95] Based on this information, I may be able to suggest one way to tie these theories together: an individual who receives little sleep for days or weeks on end may start to see signs of depression. And since more of our REM sleep occurs towards the end of a traditional 8 hour snooze, these individuals start to accumulate a sleep debt, specifically of the REM stage. So, when these individuals do find time to sleep,

they spend much more time in that REM stage that they were sorely missing. Depressed individuals who display symptoms of hypersomnia, then, perhaps can be characterized as trying to catch up on their missed sleep. To tie this in with serotonin's role in sleep, one way to view this is the idea that our bodies exhaust our serotonergic neurons throughout the day, and that REM sleep is necessary to help "reenergize" them – and this can explain why antidepressants can perhaps lower the need for REM sleep by elevating our levels of serotonin. This raises the unusual ideal of depression perhaps being the body's way of asking us to go back to bed and catch up on the rest that we have missed. Until more research is conducted on this topic, we can only continue to search for a clearer association between sleep and depression.

Research has also yielded conflicting results in the field of nutrition. For example, many studies have touted vegetarian diets as being linked with both poorer and better mental health. One 2007 study that covered more than 14,000 women over one year found that those who were vegetarian had a 10% higher chance of experiencing depression over those 12 months, as opposed to the non-vegetarians.[96] A French study completed this year found that individuals who preferred to eat only plant based products had much higher rates of depression than those who consumed animal products along with their diet. Specifically, those who ate red meat, poultry, and dairy had a risk of depression that was less than half that of the individuals who did not eat these same products.[97] However, a 2012 University of Pennsylvania study that covered almost 500 subjects found that there were no significant differences in the rates of depression between meat-eaters and vegetarians.[98] Moreover, a 2014 study found that individuals who ate meat tended to score higher on measures of stress and anxiety than vegetarians did.[99] And a 2018 study by Saghafian et al. found a strong negative correlation between increased vegetable and fruit intake and fewer symptoms of depression among a population of more than 3300 Iranian subjects.[100] Generally speaking, until more research is published into this topic, most experts would advise patients to fall back on the commonly accepted nutritional guidelines to stick to "a dietary pattern characterized by a high intake of fruit, vegetables, whole grain, fish, olive oil, low-fat dairy and antioxidants," and stay away from consuming "refined grains, sweets, high-fat dairy products, butter, potatoes and high-fat gravy," to promote optimal physical and mental health.[101]

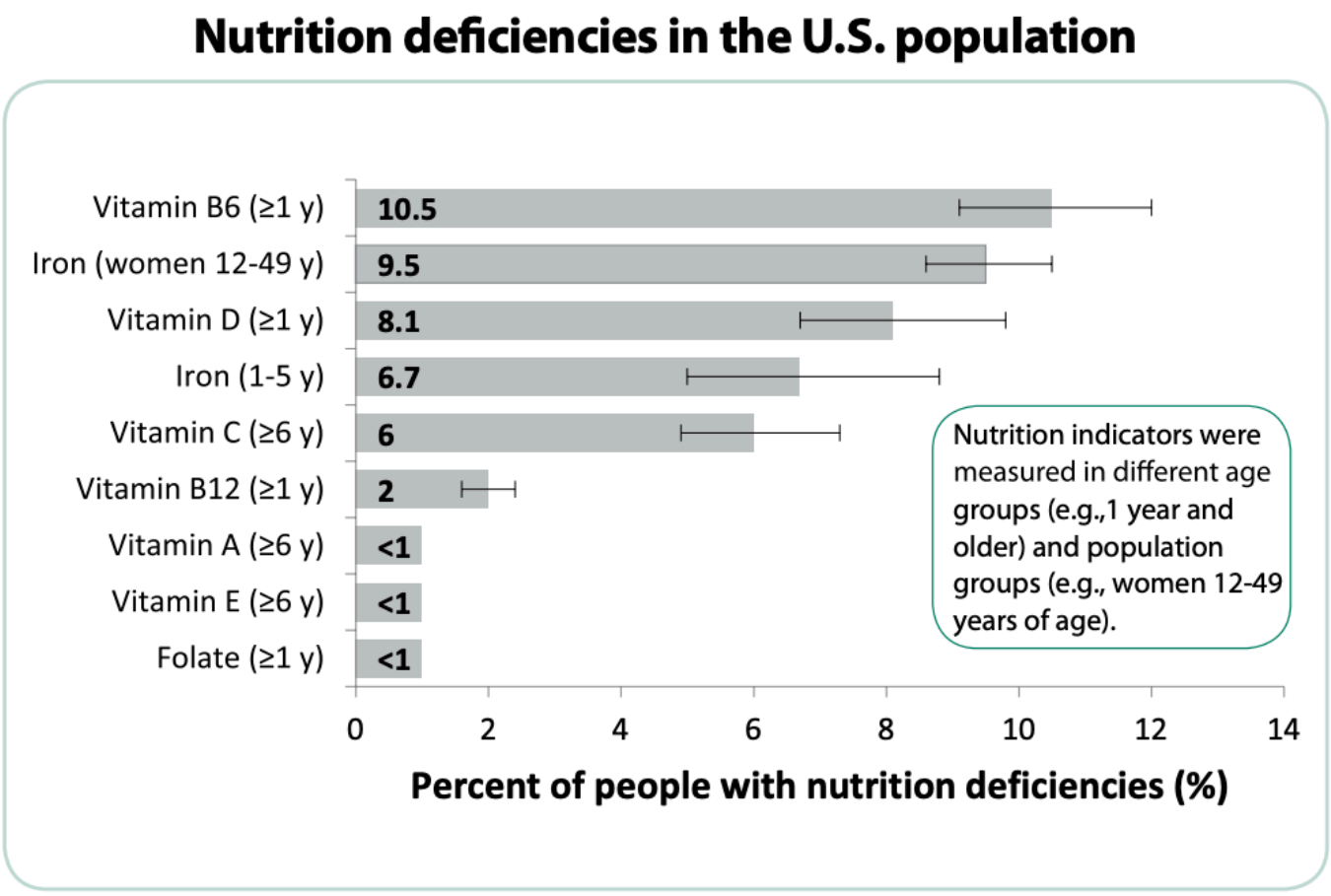
Beyond diet, some studies have looked into the efficacy of supplements in treating mood disorders. There is limited research that suggests that fish oil supplements of omega-3-fatty acids, which contain high levels of eicosapentaenoic acid, or EPA, and docosahexaenoic acid, DHA, are useful in treating depression.[102, 103] Both of these molecules are noted for their ability to lower inflammation and promote fatty acid synthesis in the brain, and have also been studied in relation to their positive effects in individuals with autism and Alzheimer's disease.[104, 105] Researchers have also found higher rates of vitamin D deficiency in individuals who are depressed.[106] Vitamin D, which is most easily obtained from sunlight, is responsible for its role in increasing bone mineral density, but also has receptors in the central nervous system, where it exerts its effects on cognitive performance, level of fatigue, and overall mood.[107] Another vitamin that should be noted is folic acid, or Vitamin B6, which is a supplement that is found in green leafy vegetables, and is a precursor molecule to nucleic acids, amino acids, and neurotransmitters like serotonin.[108] Folate deficiency is associated with anemia, or a decreased red blood cell count, which is characterized by fatigue and shortness of breath.[109] Individuals with depression tend to be deficient in folic acid, and studies have shown that when folic acid

supplements are administered in conjunction with antidepressants, experimental patients show greater rates of improvement than control subjects who used only antidepressants.[110, 111]

A 2007 report by the CDC found that about 10% of Americans were deficient in iron and folic acid, and about 8% were deficient in vitamin D.[112] The results of the report are attached below. African American populations experienced the greatest rates of deficiencies in these vitamins, possibly due to issues involving lack of access as a result of local food deserts, which may also reflect the higher rates of depression found in this community.[113, 114] Additional research is needed in this field, and future studies must place emphasis on educating the public about the importance of these vitamins on their mental health and overall well-being.

Although it can be easy to become confused by seemingly contradictory evidence in this field, it does not mean that established nutritional advice should be ignored – there is a clear link between our gut and our mind, also known as the gut-brain axis, which has amassed a growing body of research.[115] Patients with anxiety disorders also tend to describe concurrent gastrointestinal distress, and studies have shown that mice that have no gut flora are more susceptible to chronic stress and display more severe anxiety and depressive symptoms than wild-type mice.[116, 117] This field will only continue to grow in the years to come.

The remainder of this thesis will deal with exercise as a primary method of lifestyle management that has provided individuals with some success in this area.



CHAPTER 2: EXERCISE

"If exercise could be packed into a pill, it would be the single most widely prescribed and beneficial medicine in the nation."[118]

-- Dr. Robert Butler, National Institute of Aging

Although it may seem strange to other animals that our species one day decided to expend energy for fun, exercise is actually a practice that has roots in Paleolithic civilization. In fact, hunter and gatherer societies exhibited patterns of activity that involved one to two days of activity and exertion, followed by one to two days of rest, which involved cultural celebration and social gatherings.[119] This practice is very similar to what is now recommended by many medical experts, in relation to alternating periods of exercise and rest throughout the week. And as the agricultural revolution brought on the opportunity for reduced physical work, ancient philosophers and healers like Confucius and Susruta argued for the inclusion of old Paleolithic habits as a way to prevent the body from wasting away due to a sedentary lifestyle.[120]

In ancient China, the Book of Internal Medicine argued that the key to a long life was through preventive measures, which involved living in harmony with the world. Movement patterns like tai chi came about to help promote flexibility and longevity in Chinese populations. In India, the Ayurveda promoted concepts like Yoga and stretching, which created a link between breathing, movement, diet, and overall health. In many other cultures, physical fitness was also linked to social standing and provided a key link to sexual selection. For example, the importance of running and endurance was touted by several African cultures as part of the process in which boys turned into men, and attained a higher status among their tribes[121]. Notably, in Greco-Roman culture, the pursuit of fitness was seen as a noble pursuit, which was partly fueled by these cultures' focus on aestheticism.[122] The increased social status that came with an improved physique and physical performance was highly sought after, and promoted the popularity of fitness.

Today there are currently three main types of exercise that are commonly practiced across the world: aerobic exercise, anaerobic exercise, and low-intensity training.

Perhaps the most well-known is aerobic exercise, of which steady-state cardio is the most popular. This form of exercise primarily targets the cardiovascular system, in an effort to build up the individual's lung capacity and maximal heart rate by working towards the long-term goal of lowering oxygen intake during strenuous activity.[123] Running, swimming, rowing, and cycling are among the many variants practiced. Many sports, such as soccer, basketball, or even dancing, also fall into this category. In the US, running is the most commonly practiced variant, and is most often what comes to mind when the term "exercise" is mentioned. Just last year, 18.3 million people participated in marathons across the country.[124] One of the common benefits of aerobic exercise that is often cited is the "runner's high" that many runners experience after running for relatively long distances, a short term euphoria that many cite as one of the reasons they enjoy completing this often strenuous endeavor. We will explore the mental health implications of this phenomenon later in this paper.

Next, anaerobic exercise, or resistance training, is a movement that is growing throughout the world. Having especially been popularized by the bodybuilding craze of the 70's, with films like *Pumping Iron* and *Rocky*, featuring celebrities like Arnold Schwarzenegger, Lou Ferrigno,

and Sylvester Stallone, it's now a staple of many individuals' workout routines.[125, 126] The primary goal of resistance training is to increase anaerobic capacity by undergoing intense activity for a short period of time. Putting a muscle under stress builds up lactate, causes microtears in the muscle's fibers, and causes the body to repair itself to become stronger, either by reinforcing the neuromuscular connection in that muscle's motor unit, or by adding more mass in the form of added sarcoplasmic reticulum, mitochondria, or myofibrillar tissue.[127] This process is repeated in order to build up strength over a period of months or years. The fitness culture it has inspired is responsible for bringing more individuals into the gym, and for better or for worse, making people more self-conscious of their bodies, a point I will allude to later in this text. While bodybuilding is the more popular sport within the field of resistance training, weightlifting and powerlifting are two sports that have also been growing in popularity since, and are noted for their focus on pure strength over size or mass.[128]

Low-intensity movement patterns, such as walking, yoga, and stretching, are commonly prescribed to older populations, to help them get moving. Although these aren't as intense as the aforementioned exercises, they still provide their users with the benefits of injury prevention and rehabilitation, improved fitness, and often improved spirituality. Although walking is not as vigorous as undertaking more intense exercise patterns, it has still been shown to reduce the risk of many preventable diseases, like diabetes, heart disease, and high blood pressure. In fact, the Center for Disease Control and Prevention has found that individuals who walked for two hours or more per week had a 39% decreased mortality rate from all causes.[129] In the case of yoga and tai chi, these practices have not been shown to have the same effects against protection from heart disease or diabetes as walking, but their focus on balance and stability has been shown to be extremely useful – elderly populations who practiced either movement pattern actually had a decreased risk of falling than senior citizens who did not practice.[130, 131]

Of special interest to this paper, and currently growing in popularity, are high-intensity interval training regimens, or HIIT, which attempt to combine components of both aerobic and anaerobic exercise routines. They require users to undergo the short periods of anaerobic exercise required of resistance training while also requiring the limited rest time of aerobic training that helps increase maximal heart rate.[132] Much of its growth is due to the increasing popularity of Cross-Fit and competitive sports, which have helped provide millions of Americans with access to not only new and challenging workout routines, but have also provided people with supportive communities that have helped them stay motivated to continue their training sessions. For example, rugby, which is the fastest growing sport in the US, is played with bursts of starts and stops in this same way, and is especially reliant on using interval training to train its athletes.[133]

Today, however, the paradox of exercise is that although it is plastered everywhere in our society, most developing nations seem to suffer from increasing rates of obesity and cardiovascular disease. In America, fitness models grace the cover of magazines, advertisements are filled with healthy and happy models flexing their bulging muscles, and movies and television shows rely on actors and actresses showing off their seemingly perfect bodies to increase viewership.[134] But even while the idea of a fit and healthy America is shown on screen, the US is currently the heaviest country in the English-speaking world, with close to two thirds of its adult population being overweight, and half of this number suffering from obesity.[135] This is unfortunately accompanied by rises in preventable illnesses and diseases that are tied to lifestyle, such as diabetes, strokes, and coronary artery disease.[136] What's even more worrying is

that obese individuals actually spend almost $1500 more on their medical expenses per year than their healthier counterparts.[137] Ultimately, this adds to the rising cost of healthcare in the US, and accounts for about 10% the total amount spent on healthcare in this country.[138]

Why is this the case? Many individuals claim that with their lifestyles, they simply don't have time to balance this with their marriage, their jobs, their kids, and other numerous commitments. Many individuals come home from their jobs having worked extremely long hours, and are often too exhausted to even think about moving around for much longer. Others are too entrenched in their previously established habits to consider it, especially those who work sedentary jobs and may have to resort to eating sugary foods to keep themselves engaged.[139] For an example of this, we can think about toll collectors, who are required to sit in cramped quarters for most of their workdays. Others simply ignore it, brushing it aside as optional to living a healthy life, or even a waste of time. Our current president, Donald Trump, has argued against exercise, citing the idea that "the human body is like a battery, with a finite amount of energy, which exercise only depletes."[140]

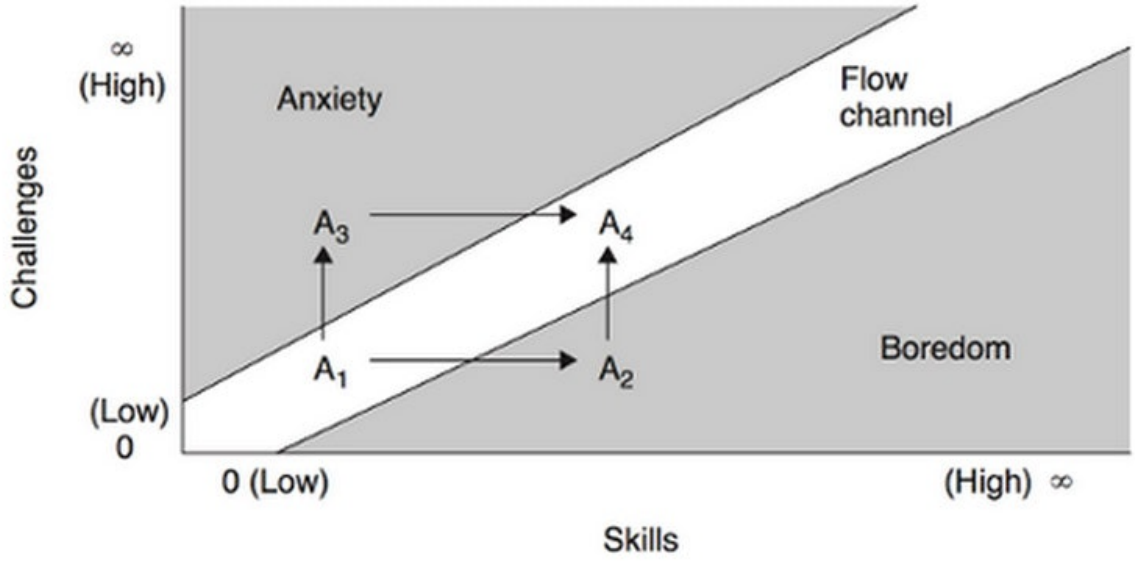
Regardless of the strange theories some individuals have about exercise, it's important to consider that many of the arguments advocating for exercise lie in its benefits to one's physical health. However, in my paper, I'd like to argue for its effects on our mental health, which I believe are even more important than its physical benefits, and perhaps may provide others with more motivation to get moving. By focusing on preventive care, we can not only improve individuals' physical health, but their mental health as well, which may prove to have greater long-term impacts down the line in their lives.

The Neurological Benefits of Exercise

The Immediate Effects of Exercise

Let's start our analysis of the benefits of physical activity by exploring what exactly is occurring in the brain immediately after individuals have exercised.

We can begin by our discussion by taking a look at cortisol. Cortisol is commonly known as "the stress hormone," and is released from the adrenal gland under durations of psychological stress. Exercise has been known to actually increase short-term cortisol secretion. While this may not at first seem helpful, cortisol in fact has its most negative effects when it is released in moderation over a longer period of time, due to chronic stress over weeks or months.[141] This can lead to the degradation of neural connections, particularly in the hippocampus, with effects such as depressive symptoms, weight gain, and increased irritability. Much of this is due to its role in decreasing the expression of BDNF, or brain derived neurotrophic factor, an important protein for neural growth that we will revisit shortly. However, a short-term increase in cortisol has the benefit of increasing cognitive capacity and enhancing one's focus.[142] A common example of this can be seen in individuals who are successfully able to focus on and complete a large number of tasks while being pressed for time, such as having to meet multiple deadlines. In looking for an explanation, it may be helpful here to apply Mihaly Csikszentmihalyi's concept of "flow," most notably illustrated by his optimal flow diagram:[143]



It demonstrates that there is a highly focused mental state that lies between the extremes of boredom and anxiety, which is the optimal mindset desired to complete the work required of us.[144] Returning to our discussion on exercise, the strenuous physical and mental exertion required by physical activity induces bursts of cortisol that are released according to the vigor and intensity of the exercise performed. This, in turn, yields the same state of focus and heightened cognitive capacity that was previously mentioned, which can explain why many individuals who exercise in the morning state that they feel more productive throughout the rest of the day. And over the long run, these effects can help dial down our body's response to cortisol release – much like how drug users build up their tolerance to a specific drug after repeated use, habitual exercise can help our body become accustomed to the corresponding release of cortisol.[145] That is, over time, it can take greater instances of psychological stress to induce cortisol release. In this way, individuals who are dealing with chronic stress can become less responsive to the stress, and can start to handle it more efficiently over time through exercise. Indeed, this decrease in vulnerability manifests itself through increases in BDNF production, opposing the degradative effects of cortisol and other glucocorticoids.[146]

In addition to inducing a heightened state of focus and decreasing psychological stress, short-term exercise has been known to produce an improved mood and feelings of relaxation.[147] One common sensation is the "runner's high," mentioned earlier in this paper, that many marathoners runners experience after about a half hour of activity. One reason this feeling occurs is evolutionary – one of the primary reason that humans were able to survive in ancient times was because of their ability to literally run down other animals – although many other species were much faster than us, our capacity for endurance allowed us to chase and exhaust our prey.[148] This ability undoubtedly was aided by endogenous compounds that allowed early humans to withstand the pain of covering such distances. At the molecular level, the chemicals that contribute to this experience include endocannabinoids and endorphins.[149]

Endocannabinoids are neurotransmitters that we naturally produce that bind to cannabinoid receptors throughout our central nervous system.[150] As these are the same ones that

are activated exogenously by THC, commonly found in cannabis, we can understand why exercise can produce similar, albeit less intense, feelings of euphoria, as the production of these compounds increases under physical activity.[151] In mice, blocking these receptors prevents the positive effects associated with the runner's high. In their work, Fuss et al. studied these receptors in mice through both the administration of cannabinoid antagonists and the deletion of their CB1 receptors, a type of cannabinoid receptor, through mutagenesis.[152] They found that both methods removed the previously measured reduction of anxiety post-exercise in mice, providing greater support for the crucial role of endocannabinoids in exercise. Applying these results to humans, one study performed by Tantimonaco, et al. determined that the levels of anandamide, one form of endocannabinoid neurotransmitters, increased in the blood plasma of subjects after exercise.[153] However, it should be noted that this exercise was done at a moderate intensity, which does tie back into the idea that the runner's high occurs at around mile six of most runners' regimens, which consist mostly of moderate steady state workouts. An added bonus of this is that since endocannabinoid levels are naturally higher in the morning than in the evening for most individuals, a well-structured morning workout can boost these levels throughout the rest of the day.[154]

The other compounds known to produce the aforementioned effects are endorphins, which bind to u-opioid receptors found primarily in the periaqueductal gray and spinal cord, as well as the nucleus accumbens, the cerebral cortex, and several tracts of the amygdala.[155] As with endocannabinoids, exercise has been found to increase the production of endorphins, which lead to commonly touted feelings of euphoria and importantly, analgesia. A 2008 study found that the regions of the brain which were most affected after a long run were subject's prefrontal cortices and limbic systems, which contained much higher levels of endorphins relative to their other cortical regions.[156] However, it should be noted that endorphins actually respond more strongly to pain, unlike endocannabinoids, which are usually released in response to stress. In this study, the runners were asked to run for 2 hours, which would usually be too intense for most individuals to handle. Another study, completed by Dinas et al., found that in physical therapy patients, B-endorphin levels increased the most with anaerobic exercise, as opposed to aerobic exercise, which had a smaller effect on these levels.[157] Therefore, it could be noted that for individuals who prefer moderate intensity, steady state aerobic exercise for a limited period of time, their "high" might come from a different source than from individuals who complete exercise with the intention of muscle fatigue, be it anaerobic strength training or aerobic exercise lasting multiple hours. That is to say, while an individual who works out casually could be enjoying a high due to a boost in endocannabinoid levels, a bodybuilder or marathon runner could experience a boost in mood due to an increase in endorphins after a painful workout. And the fact that these individuals' workout intensity serves as a threshold for the release of these compounds in the brain does make sense, considering the fact that endorphin receptors are not nearly as numerous as endocannabinoid receptors are in the brain.[158] This fact, paired with the two compounds' greater reactivity to different stimuli, can help us better make sense of how two different pathways can lead to similar experiences post-workout.

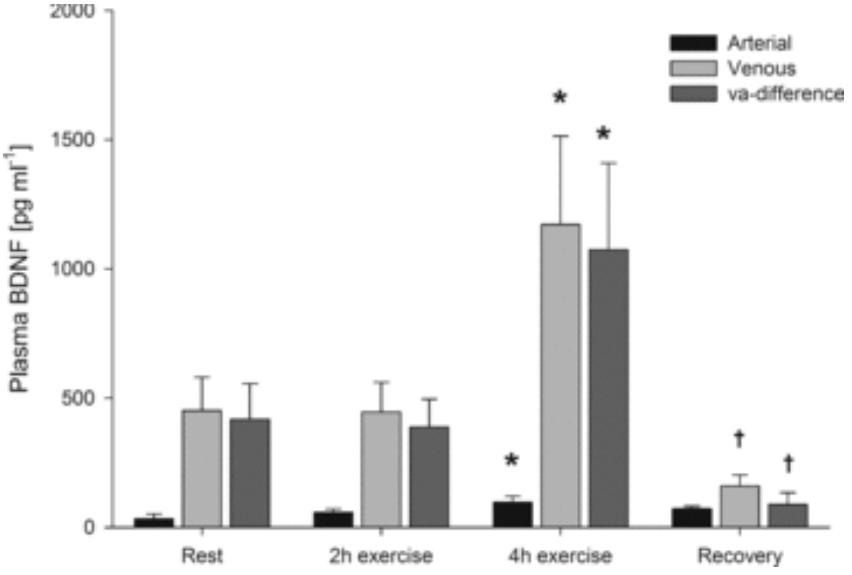
Apart from endocannabinoids and endorphins, there is evidence that a less well-known compound, phenylethylamine, plays a large role in the mood boost associated with exercise. This compound is not commonly included in such discussions because it is only present in trace amounts in the body, and has a short half-life. However, its serum levels are boosted significantly by high intensity bouts of exercise, according to Szabo, et al. As measured by

elevated urine levels of its metabolite, B-phenylacetic acid, test subjects experienced a 77% increase in this compound only a half hour after exercise. The researchers found that this compound was actually synthesized during the exercise period, which provides for an alternative mechanism to the response provided by endorphins and endocannabinoids, which take longer to start working.[159] However, due to the lack of studies done on this compound, endorphins and endocannabinoids will continue to dominate the discussion around the boost in mood conferred by physical activity.

The Extended Effects of Exercise

While the short-term benefits of exercise can provide a strong argument to motivate patients and the general public to work out when they are feeling down, its long-term effects are arguably more important therapeutically. If individuals can stick with this habit for a few months, the strongest neurological benefits will begin to take effect, most notably the structural. Whereas the short-term benefits are mostly due to temporary neurochemical changes, the structural growth associated with habitual activity is what has promoted physical activity as a promising treatment for individuals with depressive symptoms. The primary mechanism through which exercise yields these effects is by contributing to production of neurotrophic factors, which promote structural plasticity and neurogenesis in various regions of the brain.[160]

One of the most important neurohormones involved in this process is BDNF, or brain-derived neurotrophic factor. While it serves many functions, including helping to nourish existing neurons, it is most noted for its role in neurogenesis and synaptic plasticity, particularly in the hippocampus.[161] Studies have shown that exercising causes muscle cells to release proteins called myokines, including BDNF, as a response to contractions.[162] Increased levels of BDNF in the periphery, coupled with the fact that it can cross the blood-brain barrier, results in the diffusion of BDNF to the brain, and as a result, higher neural concentrations of this hormone. One study found that moderate-intensity exercise resulted in an average acute increase in BDNF of almost three times its level at rest in its subjects, as shown below.[163] More importantly, one meta-analysis of eleven studies found that habitual exercise ultimately resulted in a gradual increase in baseline levels of BDNF.[164] This increase has been shown to lead to mood improvement and stabilization, both in the long run and at the epigenetic level.



There is significant evidence to show that there is a genetic link to low BDNF production, which has been associated with greater rates of depression and anxiety. In individuals who have been diagnosed with depression, their serum BDNF levels are significantly lower than those in healthy individuals. They also tend to experience a decrease in hippocampal volume that is thought to be correlated to the aforementioned trend.[165] In fact, when researchers edited the genes of experimental mice to be heterozygous for BDNF, these animals displayed greater hippocampal atrophy and more frequent symptoms of anxiety than the control group, which was homozygous dominant for the gene. In this experiment, researchers induced a single nucleotide polymorphism, or SNP, in the BDNF gene by changing the 66th amino acid in its sequence from a valine to a methionine. After multiple generations, they soon observed lowered BDNF synthesis as well as impairment of hippocampal functioning, as measured through tests of working memory. What is surprising is that this does not necessarily predict depression or anxiety in individuals – rather, it predicts a higher sensitivity to external stressors, which is correlated with greater release and systemic proliferation of cortisol.[166] This point has important implications for how therapists can best aid their clients, a point we will return to later in this chapter.

Further epigenetic studies show that BDNF production can be altered by the activity of MeCP2, a protein that blocks BDNF promoter IV in the genome. Under normal conditions, the increase in intracellular calcium resulting from neuronal depolarization causes MeCP2 to be phosphorylated. This demethylates the promoter region, which removes its blockade and allows BDNF to be transcribed and synthesized. However, under stressful situations, the BDNF promoter region undergoes increased methylation, which induces greater MeCP2 blockage of that region. Not only does this prevent BDNF production, it leads to decreased hippocampal activity and increased symptoms of depression.[167]

Of special note is BDNF's impact on serotonergic neurons. As discussed previously in this paper regarding the monoamine hypothesis, lower serotonin levels have been implicated in depressive disorders, and many anti-depressants target the release and reuptake of this neurotransmitter at the synaptic level. One study analyzing two such antidepressants, Mirtazapine and Imipramine, found that their administration led to an increase in BDNF synthesis in rats, especially in their hippocampi and cerebral cortices.[168] Mirtazapine normally acts as a post-synaptic 5-HT_{2A} (serotonin) receptor antagonist and reverse agonist, and both inhibits the sensitivity of the post-synaptic neuron to serotonin and allows the neurotransmitter to stay in the cleft longer.[169] Interestingly, the increased levels of BDNF bolster the effectiveness of the drug by downregulating 5-HT_{2A} receptor synthesis, providing for a stronger inhibition of depressive symptoms through long-term administration of the drug. This experiment has exciting implications, because it suggests that extended mirtazapine use has the potential to increase the expression of the BDNF gene, which can provide a protective effect for future generations.

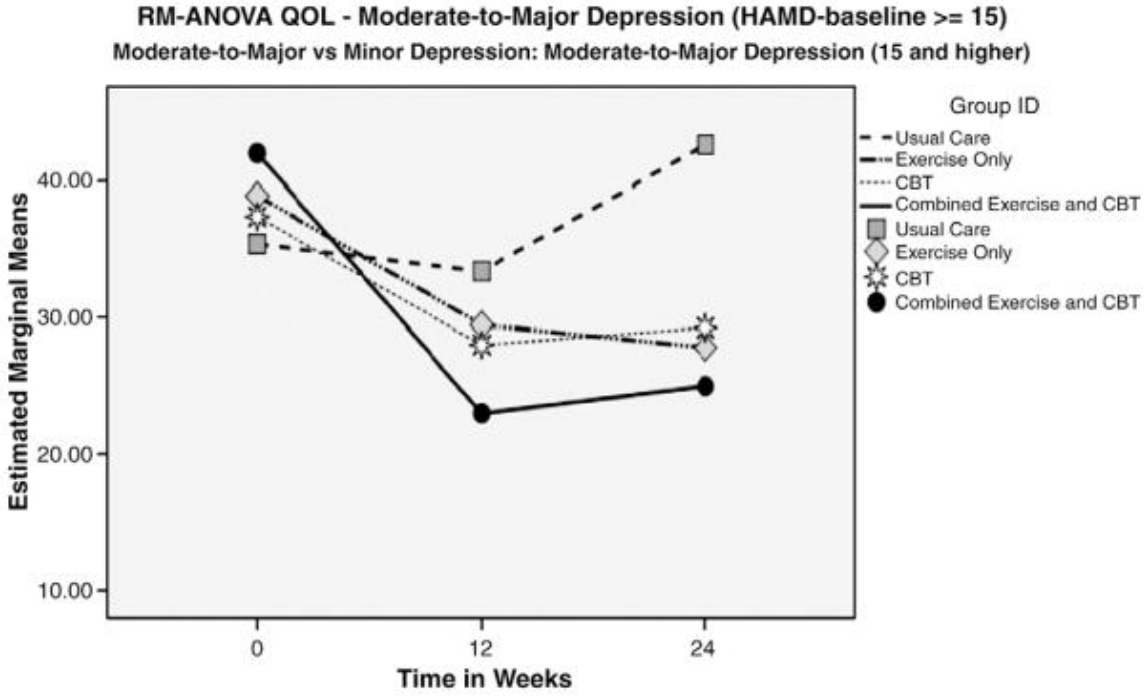
Another important protein to include in our conversation about myokines like BDNF is irisin, which plays an important role in hippocampal neurogenesis. While physical exercise helps generate new neurons, it is actually a little known fact that about half of these neurons undergo apoptosis, or programmed cell death, after only a few weeks of their generation.[170] Irisin's role in this process is to extend the lifespan of these neurons by inducing their proliferation and increasing their differentiation, so as to keep them functioning for longer periods of time. One study that analyzed FNDC5, a precursor to irisin, demonstrated that decreasing the synthesis of this precursor resulted in a marked decrease in neural stem cell differentiation in mouse

embryos.[171] And in their study on neurogenesis, Moon et al. demonstrated that irisin is responsible for increasing cell proliferation, and also promotes STAT3 signaling, a transcription factor that promotes cell growth.[172] In other words, irisin is one of the factors responsible for the commonly known principle "use it or lose it," which requires that neural connections must be regularly exercised in order for our brains to maintain their connections within our circuitry. This can provide further evidence for why physical activity must occur consistently in order to see long-term improvements in depressive symptoms over time.

Another protein that is affected by exercise is VEGF, or vascular endothelial growth factor. Although this has primarily been studied in its role in promoting some types of cancer, its function actually can be beneficial after the body has undergone physical stress. The production of VEGF is triggered in muscular tissue under hypoxic conditions, when cells of a particular region are starved for oxygen - the proteins quickly cross the blood brain barrier and bind to neural and glial receptors, and facilitate oxygen transport to these cells to protect them. VEGF does this by acting as a vasodilator, increasing endothelial permeability and promoting blood flow to these regions.[173] This greatly speeds up their process of repair and promotes cell growth in affected areas. In this context, it would make sense then, that the shortness of breath and rapid increase in heart rate directly caused by exercise can help promote the proliferation of these factors. These effects are especially salient in the hippocampus, which is one of the few areas of the brain where neurogenesis can occur, and as discussed above, is especially vulnerable to such fluctuations in key protein serum levels. In Fabel et al's study of hippocampal neurogenesis, the researchers measured the stress hormone levels of resting lab mice and compared them to lab mice that were required to run. While neither group experienced a decrease in their average stress-hormone levels, the experimental group displayed hippocampal neurogenesis at twice the rate of the control group, and exhibited highly elevated VEGF levels. Blocking VEGF from passing through the blood brain barrier resulted in a significant decline in induced neurogenesis in the mice who ran, although it did not have any effect on the mice at rest. This proved that aerobic exercise caused this increase in VEGF, and was an effective way to promote hippocampal growth and optimal health.[174] In fact, there is evidence to show that VEGF is one of a few proteins that becomes highly promoted after CNS injuries for this very reason, although the research into this field is very limited.[175] Further study must be completed to better understand these mechanisms.

Structurally, exercise also produces an increase in the volume of grey matter in almost all areas of the brain, including the hippocampus, which plays a role in memory formation, and the nucleus accumbens, which is involved with motivation and reinforcement. Most notably, it also increases the cortical volumes of the anterior cingulate cortex, which is responsible for decision-making, emotion, and ethical reasoning, and the prefrontal cortex, which oversees our higher order skills such as decision-making and behavioral inhibition.[176] In fact, these improvements can be seen in both short term and long term appraisals. One such study found that decision-making and problem-solving skills in children improved immediately after a short period of exercise, and that their general attention span also improved after exercise was implemented as a habit – we will revisit the specifics of this study later in this paper. Although it may seem fit to ignore cognitive improvements in a thesis that focuses on individuals' emotional states, better cognitive skills are crucial in helping depressed individuals recover from their symptoms. The improvements in executive functioning can aid individuals who use cognitive behavioral therapy by allowing them to be more rational and balanced with their appraisal of their current situations.

CBT requires its patients to identify negative thoughts and beliefs and better analyze and regulate them to ultimately improve the way they cope with their emotions. So, any method that would allow patients to view their thoughts in a more analytical and educated manner would be ideal. And this has, in fact, proven to be the case: numerous studies have shown that depressed patients who were treated using both CBT and exercise regiments improved faster and more significantly than patients who were treated using only CBT or only exercise.[177, 178] A graph of Gary et al.'s results is included below. Another study by van Koulil et al. on patients with fibromyalgia concluded that "the combination of CBT and exercise training is the most effective treatment" for reducing depressive symptoms, even over pharmacological treatments like tricyclic antidepressants. One of the reasons cited was that the treatment effects of pharmacological interventions may disappear faster after treatment is stopped, compared to the effects of non-pharmacological methods, which last much longer after their regimen is dropped.[179] This may be in part due to patients' conscious and unconscious retention of cognitive methods and techniques, as well as their possible greater adherence to them.



While we have touched upon the most important biological factors involved, there are still a multitude of other noteworthy proteins and hormones that should not be ignored in future discussions of the subject. These include insulin-like growth factor 1, adenosine, atrial natriuretic peptide, and protein fosB, all of which would warrantee further review in any other analysis of this material.[180, 181] With this clinical knowledge in hand, let us now move to a more practical discussion of the clinical trials that have analyzed the effectiveness of exercise in depressed patients - do the theories we've discussed have any merit in the real world?

The Efficacy of Exercise in Clinical Trials

Steady State Aerobic Training

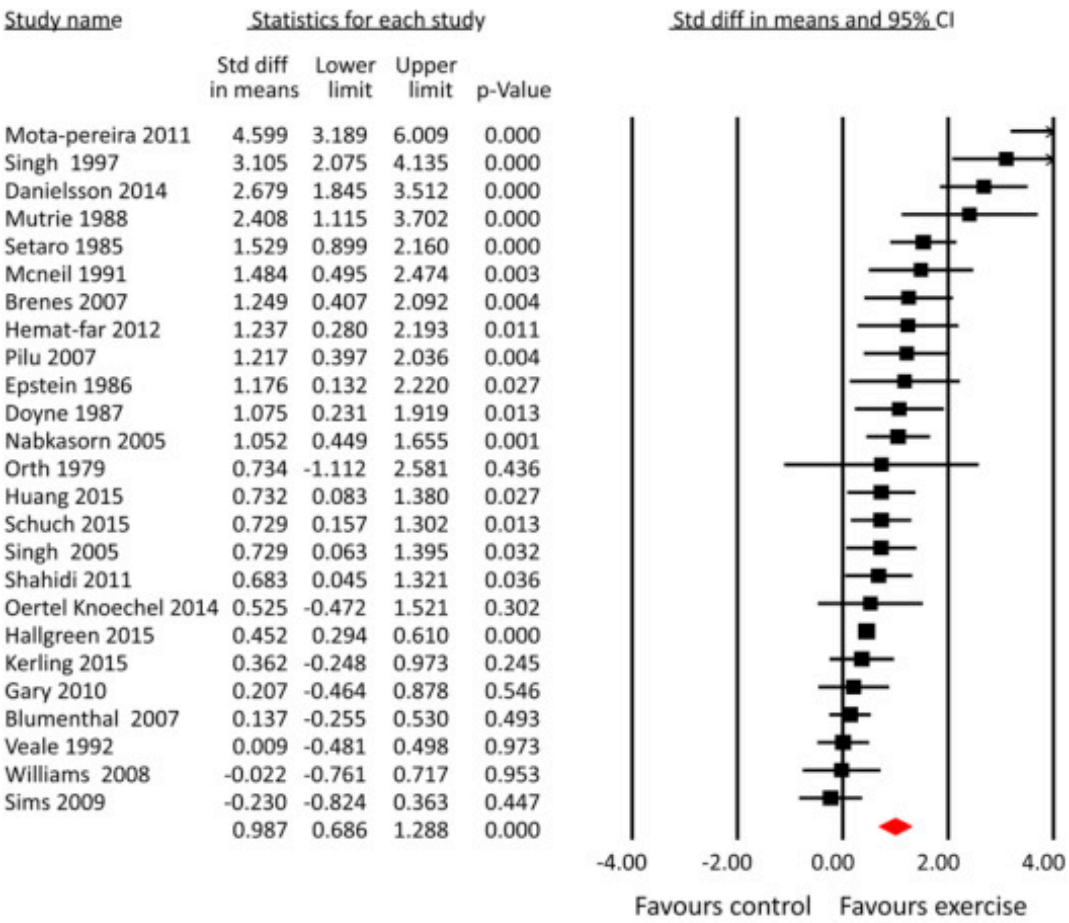
The simplest advice to give to someone who wants to treat their mental health is to encourage them to just start exercising. Simply being in shape physically is strongly correlated with a reduced risk of developing clinical depression. A 2016 public health review collected data from studies that cumulatively involved more than 1 million adults, and divided their data into thirds based on the relative cardiorespiratory fitness of the subjects tested. It found that the men and women in the healthiest third of individuals sampled were 75% less likely to develop depression than the least healthy third, and that the middle third had a 23% greater chance of developing such symptoms than the healthiest group. Another meta-analysis published that same year demonstrated that moderate to intense bouts of exercise served as effective therapy for dealing with mild to moderate depression and depressive symptoms. Although its sample size was smaller than the former study, it still demonstrated that there was a causal effect of exercise on better overall mental health.

Most of these studies do not differentiate between types of exercise, however, and tend to generally focus on aerobic exercise, perhaps because this is one of the simplest and most accessible form of exercise patients can complete. Unlike resistance training, aerobic exercise does not require as much training on proper form, and is not as complex. And most studies do show quite a bit of support for the benefits of aerobic exercise – a study discussed at the American Physiological Society has hypothesized that one of the reasons it is so effective is because more so than other forms of exercise, aerobic exercise increases blood flow to the brain, providing it with more oxygen and nutrients than other forms of activity. By using ultrasound testing to measure arterial flow, researchers discovered that running triggered greater blood flow than walking or standing[182]. These results are even clearer when paired with the findings of a longitudinal Norwegian study that analyzed more than 30,000 adults over an eleven-year span, and discovered that individuals who exercised for even an hour every week experienced reduced depressive symptoms compared to those who did not. The effects were compounded for participants who chose to exercise more frequently and more vigorously.[183] In trying to understand these effects, researchers studying mice have found that running activates the region of the hippocampus that is responsible for spatial recognition – this in effect acts to protect against hippocampal atrophy, and may also be one of the primary reasons why people score higher on cognitive tests immediately after their workouts.[184]

And these results seem to be working for individuals who have been struggling with antidepressants or other forms of treatment. A meta-analysis compiled by Morres et al. concluded that aerobic exercise "emerged as an effective antidepressant intervention." In this study, it was found that patients who completed an average of 45 minutes of exercise, 3 times a week, for about 9 weeks, demonstrated significant antidepressant effects, supporting the utility of aerobic exercise as a primary treatment option for patients.[185] Interestingly, one study completed by Brazilian scientists found that after a four-week aerobic training protocol, patients who completed the requisite training required lower doses of their antidepressant, a selective serotonin reuptake inhibitor known as sertraline, than did the control group. 52% of the patients required only 50mg of their usual 100mg dosage, while 31% of patients now required no dosage to maintain their health.[186] The scientists argued that one of the main reasons for this was the patients' improved cardiovascular fitness. The studies they cited had found that on average, a

low maximal oxygen capacity was associated with more severe depressive symptoms in men, and that greater cardiovascular fitness was correlated with fewer symptoms of depression.[187, 188] Regardless, the impressive outcome of the study shows that for individuals with treatment-resistant depression, there are still options that they can choose that may be able to alleviate their symptoms. In addition, this can provide a large socioeconomic benefit for patients who may be struggling to afford their medication – being able to lower the required doses could cut medical costs in half for patients. However, more research must be done to better understand the effectiveness of exercise in relation to other forms of antidepressants, and get a clearer understanding of its true impact in this area.

In comparing the efficacy of aerobic exercise to pharmacological options of treatment, Yael Netz, an Israeli researcher, conducted analyses of both randomized control trials and other meta-analyses. With respect to the RCT's she studied, she found that "exercise and standard antidepressant treatments were equally effective." Comparing the meta-analyses provided similar results, and she stated "support [for] the use of exercise in the treatment of depression, at least as an add-on therapy."[189] Multiple studies have corroborated these findings, and have provided support for the immense benefits conferred by aerobic training for individuals with depression.[190, 191] The results of Schuch et al.'s meta-analysis are attached below. While experts would not recommend it as the preferred treatment option for mental health patients, it is clear that it is an extremely valuable complement to existing therapeutic methods.



Std diff in means = standardized differences in means, CI = Confidence Interval

Resistance Training

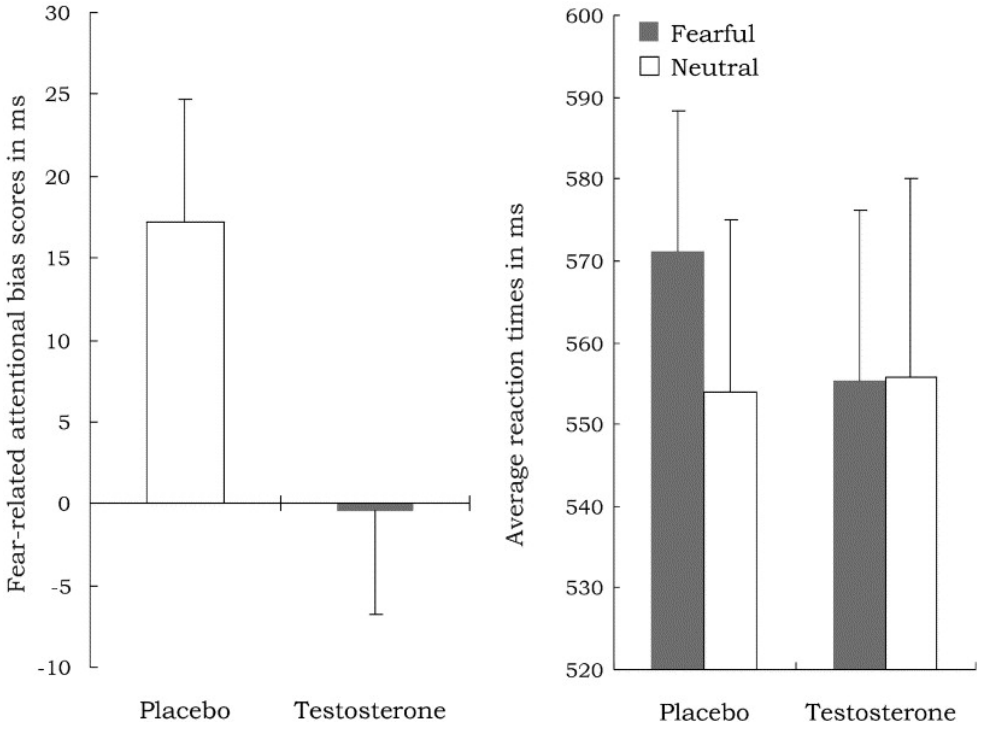
Now that aerobic exercise has proven itself as an extremely useful tool in fighting depression, we must take a look at how resistance training stacks up against it. One study published in the *Journal of the American Geriatrics Society* found that senior citizens with mild cognitive impairment who lifted weights twice a week for six months performed better at multiple cognitive tests than subjects who only completed stretching exercises during same time frame. This improvement was apparent not only immediately after the study, but also retained for up to twelve months after the study had ended, while the group who stretched displayed a slight decline in their performances over time, which shows that stretching was not enough to ameliorate the natural progression of age-related impairment. Interestingly, there was also a positive correlation between the amount of strength gained and the improvement in cognitive performance.[192] Although we cannot establish a relationship beyond correlation, these two trends once again highlight the importance of consistency in training, and demonstrate that the long-term effects hold significant weight in the improvement of multiple benchmarks in these individuals.

A meta-analysis by O'Connor et al. of four studies focusing on resistance training in depressed psychiatric patients reported an across-the-board improvement in depressive symptoms, with patients who completed only resistance training showing a larger improvement than patients who completed only aerobic training. The analysis also found that strength training was effective in improving depressive symptoms in college students and police officers, as well as in patients with osteoarthritis, fibromyalgia, and spinal cord injuries.[193] Another meta-analysis of 33 studies, with a sample size of 1877 patients, also found the same results.[194] Importantly, it also found that subjects who were already mentally healthy before participating in the studies ended the experiments with a greater resistance to environmental stressors, spent less time ruminating, and were more capable of emotional regulation than their counterparts in the experiments' control groups. The study also identified many factors that did not make a significant difference in the patients' mental states, including their age, the particular training program they used, and the amount of time spent per visit, implying that simply undergoing any type of resistance training has a relatively positive impact on patients – this is good news for individuals who may have different goals in mind, and thus may want to train accordingly. However, the study also found that the individuals who showed the greatest improvements were those who were suffering from more severe depression, which suggests that to treat such patients, exercise needs to be addressed as a top priority, and should supplement other concurrent forms of treatment.

While I have spent much of my paper discussing depression, there is growing evidence that anaerobic training may also prove useful for individuals with anxiety, which I believe should not be ignored in such conversations. In their paper, "The Impact of Aerobic and Anaerobic Exercises on the Level of Depression, Anxiety, Stress, and Happiness of the Non-Athlete Male," Kianian et al. designed an experiment to determine the effects of the various training regiments on a variety of psychological and physiological markers in patients.[195] Surprisingly, the group found that ten weeks of anaerobic exercise was significantly more effective in improving symptoms of anxiety in patients than was ten weeks of aerobic training. As it turns out, one of the key reasons why resistance training is so effective in this arena is because it increases serum testosterone levels in subjects. In Aikey et al.'s study of the effects of testosterone in mice, researchers found that male mice reflexively released testosterone during sexual encounters that

later reduced their anxiety, as measured by their performance on elevated plus-maze tests. Over a series of eight experiments, the researchers determined that exposure to female urinary pheromones had the same anxiolytic effect over a half-hour period as produced by injections of testosterone. It's important to note here that these effects were dose-dependent, as control mice and subject mice who received less than 250 micrograms of testosterone showed no reduction in anxiety.[196] Another study completed the following year demonstrated that lower doses did produce the same effects, but only after repeated daily administrations of this compound.[197] A later pharmacological analysis showed that in these experiments, testosterone was converted into several different types of neurosteroids, including androsterone and 3-alpha-androstandione, that later upregulated GABA receptor signaling. As it has been hypothesized that GABA receptor dysfunction is one of the key drivers of anxiety disorders, the results of this experiment further strengthen this hypothesis.

In human trials, Van Honk et al. demonstrated that injections of testosterone administered to female subjects tended to decrease their unconscious anxiety, but not conscious fear, as measured through the Stroop test.[198] It is important to note that in this study, the injections consisted of only 500 micrograms of testosterone, which was same amount given to the mice in the earlier experiments – perhaps larger doses would elicit greater anxiolytic responses, although in this context it would seem that dampening unconscious feelings would be more beneficial to mildly anxious individuals than simply reducing conscious fear, which is often biologically necessary around dangerous objects or situations. This does raise the possibility of research into phobias, and whether adding greater amounts of testosterone may aid people with such conditions. Some of the results of this study are attached below:



The positive impact of resistance training on testosterone production, and the production of related hormones like growth hormone, GH, has been established for quite some time. One study of many, completed in 1989, analyzed differences between young subjects, with an average age of 23 years, and older subjects, with an average age of 63 years, in how their serum growth hormone levels responded to resistance training.[199] Craig et al. showed that by far the younger individuals benefited the most from such training, with their growth hormone levels rocketing from around .85 ng/mL pre-training to about 8.61 ng/mL post-training. This level of responsiveness was not seen in the older group, whose GH levels rose from 1.00 ng/mL before training to about 3.43 ng/mL after training. Although not as impressive, this study is promising for older individuals who are unsure of how to utilize resistance training, or perhaps may feel that they are past their prime – there clearly is still much more room to increase the serum levels of these important compounds, and individuals should be encouraged to try resistance training if it is possible for them to do so, regardless of their age.

Related research in mice has shown that the administration of 3-alpha metabolites is responsible for this improvement in cognitive functioning, and alleviation of depressive symptoms. This was demonstrated in lab mice through forced swim, water maze, and avoidance tasks. In testing older mice, researchers found that negative ailments increased with age, which also was correlated with a decrease in 3-alpha-diol production.[200] When paired with the above study, this provides further reinforcement for the need to integrate resistance training in patients' routines, especially as they grow older. One particular factor to consider is that older individuals tend to display unconventional symptoms of depression, including irritability and talkativeness, which are similar to the symptoms displayed by patients with anxiety disorders. Perhaps this may explain the findings of a 2014 study that found a negative correlation between serum testosterone levels and severity of depressive symptoms in older Iranian men. The healthier men displayed testosterone levels of about 4.94 ng/mL on average, while the men with depressive symptoms had levels closer to 4.20 ng/mL, on average. In fact, these men's levels of testosterone had a greater relationship with their depressive symptoms than age, educational levels, or even single-residency status.[201]

With respect to the benefits of exercise outside of depression and anxiety, many studies have shown the benefits of completing both aerobic and anaerobic training. While aerobic training has been linked to improved performance in cognitive tasks, especially ones that measure executive functioning, anaerobic training has been implicated in improved executive functioning and working memory.[202] Through our discussion of both types of training methods, it is clear that to promote healthy mental functioning, both aerobic and anaerobic training systems must be implemented into individuals' routines.

High Intensity Interval Training

With the results of these studies now at the forefront of our discussion, I believe that we can build upon them to make a strong case for high intensity interval training as a method to get the best of both worlds.

For one, HIIT seems to promote blood flow to the brain just as well as steady state training, as demonstrated by multiple studies. One 2007 study completed on patients who had previously experienced heart failure demonstrated that interval training resulted in a 46% increase in maximum oxygen consumption over continuous training, which resulted in a 14% increase. On top of this, left ventricular ejection fraction, a measure of heart strength and resultant blood flow, increased 10% more in the group that underwent interval training than in the group that completed continuous training.[203] Other studies have also supported the use of HIIT training to aid patients with cardiovascular issues, citing that while the difference in aerobic improvements was not as strong as in the aforementioned study, the amount of time that patients can save in completing shorter workouts does make them preferable to standard endurance training.[204] In one recent study, Foster et al. tested more than 50 untrained college students over an eight-week period by asking them to complete either 20 minutes of steady state training or eight intervals of 20 second sprints with 10 seconds of rest on stationary bikes. The researchers found that the students who completed sprint training demonstrated a 24% increase in their maximum oxygen consumption as compared to the steady state group, who demonstrated a 17% increase from baseline oxygen consumption prior to training, which is another measure of aerobic endurance.[205]

Measure		**Pre Training**	**Post Training**	**Change (%)**
VO_2max (ml·kg^{-1})	Steady-State	33.6 (5.4)	40.1 (6.3)	19% *
	Tabata	34.0 (6.5)	40.1 (6.8)	18% *
	Meyer	34.3 (9.1)	40.6 (8.7)	18% *
P_{aer}PO (W·kg^{-1})	Steady-State	2.65 (.61)	3.09 (.76)	17% *
	Tabata	2.72 (.77)	3.36 (.69)	24% *
	Meyer	2.81 (.70)	3.21 (.69)	14% *
Wingate PPO (W·kg^{-1})	Steady-State	11.5 (1.6)	12.4 (1.4)	8% *
	Tabata	11.7 (1.4)	12.7 (1.4)	9% *
	Meyer	11.8 (1.5)	12.4 (1.7)	5% *
Wingate MPO (W·kg^{-1})	Steady-State	6.1 (1.0)	6.3 (.9)	4% *
	Tabata	6.4 (1.0)	6.9 (1.1)	7% *
	Meyer	6.2 (1.3)	6.6 (1.0)	6% *
Combined Exercise	Steady-State	6.75 (1.07)	7.26 (1.02)	7.6% *
Capacity (W·kg^{-1})	Tabata	6.94 (1.06)	7.65 (1.06)	10.2% *
	Meyer	6.94 (1.17)	7.40 (1.13)	6.6% *

One of the more interesting points about this experiment was that although all the students who started the experiment were able to participate until its conclusion, the level of interest of those in the interval-training group declined significantly throughout the eight-week period. The participants cited the intensity of the exercises as one of the primary factors discouraging them from utilizing it for personal use in the future. An important factor that played into this was the fact that these students were relatively untrained before starting this routine, which perhaps was too strenuous for beginners to undertake. This is something that therapists and clinicians must take into account if they wish to maintain, and ideally improve, their patients' motivation when prescribing such workout routines. While studies have shown that the intensity of exercise undertaken may correlate to improved outcomes, being enthusiastic about moderate-intensity exercise and completing it consistently is better than quitting half-way through an intense program.

Moving back to our comparison, HIIT also increases serum testosterone levels much more significantly than steady-state training. A 2012 study measured the difference in testosterone response between interval exercise (IE) and steady-state endurance exercise (SSE) in 15 runners, and found that IE significantly increased free testosterone post-exercise in comparison to SSE. However, measurements taken 12 hours after each trial displayed a drop in free testosterone for the men who completed interval training – instead, their levels of 3-alpha androstanediol were elevated, the same testosterone metabolite implicated in our discussion regarding the anxiolytic effect of resistance training.[206] In other words, the testosterone wasn't simply floating around in the blood – it was actively being metabolized and utilized for growth by androgen-sensitive tissues. Another study completed by Herbert et al. demonstrated that these same effects were long-lasting. After asking 17 athletes to utilize a nine-session HIIT sprint regimen for six weeks, the authors compared pre-HIIT and post-HIIT serum testosterone measurements. They found an increase in free testosterone from 7 ng/mL to 7.5 ng/mL over the six-week period, which illustrates that the potential for the protective effects of testosterone increases with consistent exercise.[207] With this being said, a potential issue of these experiments with regards to this thesis is that the former have focused mostly on experienced athletes, who perhaps were already more responsive to testosterone, or already had relatively high levels of testosterone to begin with.

So, when the same research group conducted similar studies on untrained, sedentary men using an exercise bike, they found that aerobic training produced no increase in bioavailable testosterone, while high intensity interval training increased their levels from 6.6 ng/mL to 7.3 ng/mL over a 12 week period.[208, 209] Most importantly, this study analyzed 22 men who were all older than 60 - this news is promising for individuals who worry that their level of experience may be a limiting factor, or are afraid that it may be too late to start such training routines to see their rewards. However, it should be noted that this group was trained for 12 weeks, rather than 6, as the athletes were, which does indicate that perhaps a longer and more consistent training period is required to experience these positive effects. In such cases, it's important to ensure that older populations, whose bodies are not as responsive to testosterone as those of younger patients, are assisted in developing a plan that can allow them to be consistent and patient with their training. Importantly, the positive effects of training on testosterone production have also been observed in women - one randomized controlled trial found that women who underwent either resistance training or endurance training both displayed a significant increase in acute testosterone production over women in a control group.[210] However, this study was limited in

scope, as it did not observe long-term effects of consistent training, and did not test for high intensity interval training. This highlights the need for more research to be completed in the area of women's athletics to ensure for a more complete understanding of these biological mechanisms.

As HIIT promotes the physical benefits of both types of training, it should follow that the neurological benefits are significant as well. A recent study from the University of Basel tested patients suffering from major depressive disorder, and found that sprint interval training resulted in a meaningful decrease in patients' scores on the Beck Depression Inventory, from an average score of 31 down to 18 over a four-week period, as compared to a 10 point decrease in patients who completed steady-state training over the same time period.[211] The authors hypothesized that one of the reasons for this decrease was because of the greater intensity of the interval training, which has been found to correlate positively with increased BDNF production. While it is not currently possible to observe BDNF interactions at the molecular level in humans, studies completed on mice have shown that HIIT training does work – the levels of mature BDNF observed in depressed mice increased significantly following a four week period, while precursor BDNF molecules decreased in number – this ratio was used as proof of HIIT directly being responsible for this increase, while behavioral tests proved that the mice displayed less anxious and more exploratory behavior, along with more movement, upon conclusion of the training period.[212]

Numerous studies have also tied HIIT training to improvements in anxiety in human patients. One study comparing high intensity exercise to low-intensity training found that the former was correlated with a reduced sensitivity to anxiety inducing situations, as well as a decreased physiological response.[213] This was demonstrated in both acute measurements and in a one-week follow-up. Importantly, this reduction in anxiety is often correlated with a corresponding decrease in depressive symptoms. A recent study started this year on patients with panic disorder demonstrated that over only a twelve-day period, patients' scores on the Beck Depression Inventory almost halved from 21.2 to 10.9.[214] The researchers are currently investigating the long-term effects of this finding, to determine if these effects are long-lasting enough to translate into clinical use. An Australian research team undertook a similar task in their 2005 study comparing how elderly patients with depression fared under conditions of high intensity training, low intensity training, or standard care by a general practitioner. They assessed for at least a two-fold reduction in the patients' scores on the Hamilton Scale of Depression. In doing so, they found their desired results in 61% of the high-intensity group, but only 29% of the low intensity and 21% of the standardized care group.[215] Although these results are promising, what is even more important is the fact that these effects were more significant in individuals who were experiencing more severe symptoms of depression, as opposed to those who were facing milder symptoms. This lines up well with our earlier assertion that the effects of exercise are intensity-dependent, and that individuals who are experiencing more severe symptoms need a greater stimulus to experience the benefits that someone with milder depression can gain through lower intensity training. Interestingly enough, one statistic that the study cited was the effectiveness of placebo medications (30%) in treating patients with major depressive disorder, which seemed remarkably similar to the percent of individuals who benefited from low intensity exercise (29%).[216] In fact, when the authors looked into this factor, they actually found that most

of the patients who believed that exercising could help were the same patients who benefited the most from low-intensity exercise. This belief was not strongly correlated with the effectiveness[217]of high-intensity exercise, however. The results of this study are attached below.

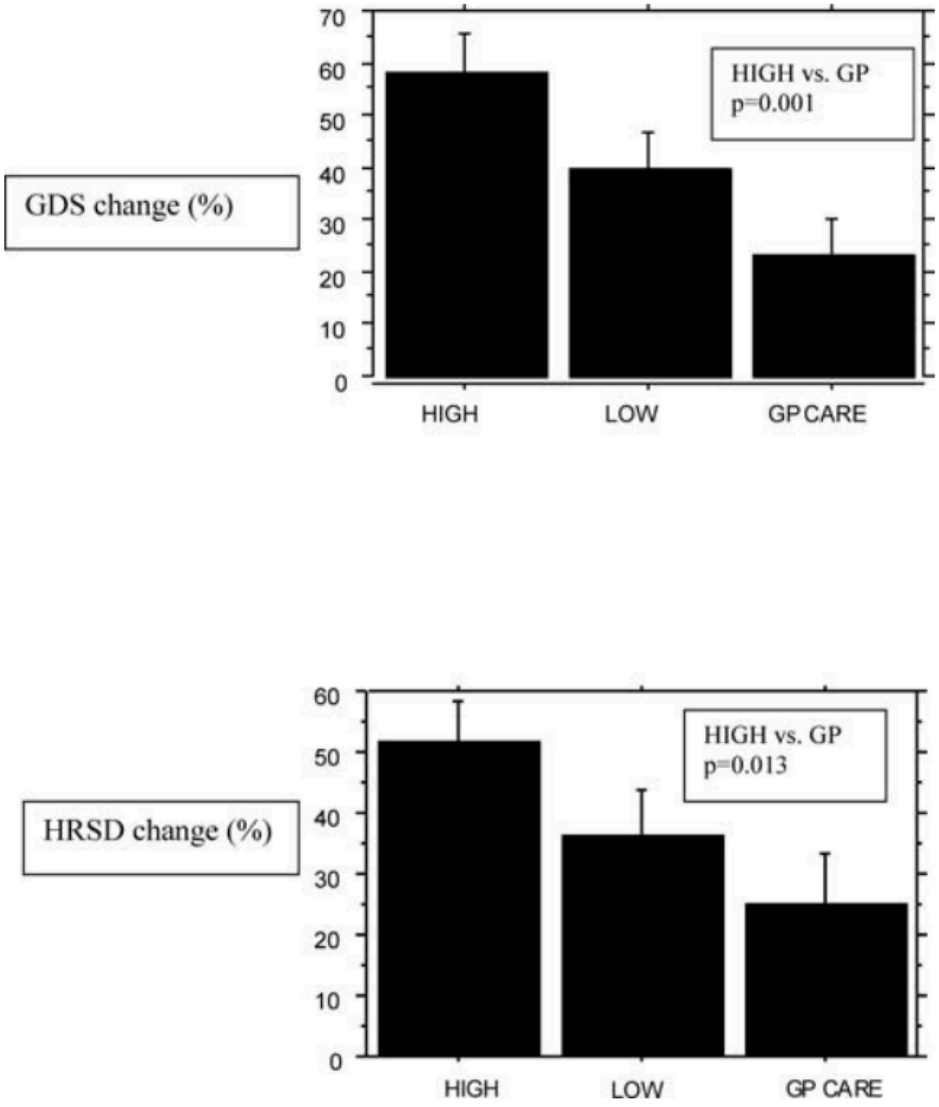


Figure 2. Relative change in self-rated and therapist-rated depression scales in the three study arms. Results were analyzed by analysis of variance (ANOVA) and post hoc t tests. **Top:** Reduction in self-rated depression. GDS = Geriatric Depression Scale; HIGH = high intensity progressive resistance training; LOW = low intensity progressive resistance training; GP = general practitioner standard care. $p = .004$ (ANOVA for group effect); $p = .001$ (HIGH vs GP; Fisher's protected least significant difference post hoc t test). **Bottom:** Reduction in therapist-rated depression. HRSD = Hamilton Rating Scale of Depression; HIGH = high intensity progressive resistance training; LOW = low intensity progressive resistance training; GP = general practitioner standard care. $p = .044$ (ANOVA for group effect); $p = .013$ (HIGH vs GP; Fisher's PLSD post hoc t test).

These results provide an encouraging prognosis for those struggling with milder forms of depression – in shaping their therapeutic plans, they may be more easily able to reap the benefits of therapy that is supplemented with exercise, and ideally may be able to stay motivated much longer than others. However, therapists must be able to deal with these patients' suggestibility in a skilled manner, so as to not unwittingly provide unrealistic expectations regarding the success of such routines that may prove disappointing for their clients in the long run. Moving to a broader vantage point, another takeaway from this study is its sociological implication – the authors pointed out that annually, only a little more than 20% of individuals with depression receive mental health treatment that they would classify as "adequate" from their providers. 25% of older adults who are receiving antidepressants to help treat their depression end up dropping out of such trials.[218] And of the individuals in the study's general care group, only about half of these individuals were even offered pharmacological treatment or general therapy, rates which are similar to the care given across the U.S. In instances such as these, high intensity exercise seems to make a case for its efficacy over traditional treatment methods. Not only did this study demonstrate that high intensity training was more beneficial than general treatment, it showed a promising route for individuals who want more options to care for themselves, and now may not have to rely as much on professionals who may not be providing them with satisfactory care.

Importantly, HIIT training can be utilized across all age groups – research focusing on children is currently underway, with the hopes that it may safeguard the public from developing illnesses like depression in the future. Moreau et al. tested interval training on executive functioning in 318 children, and discovered that even 10 minutes of exercise boosted working memory and attention span in the training group.[219] Children in the control group instead played computer games or took quizzes for the 10-minute period, and did not display a significant increase in cognitive reasoning ability directly after the period. Most importantly, however, the authors of this study also took care to genotype the children before starting their study, and found that children who were homozygous for the variant of BDNF containing valine at the 66th amino acid position (BDNF val^{66}) did not benefit as much from exercise as individuals who were heterozygotes for this BDNF allele and contained methionine at this position. As mentioned in our previous discussions regarding this polymorphism, individuals with BDNF met^{66} tend to express lower levels of baseline BDNF, but are more responsive to exercise in general than BDNF val^{66} homozygotes.[220] From a therapeutic and public health standpoint, this is extremely important for us to consider when thinking about how to combat depression – we need to place greater emphasis on individuals who may be at higher risk of developing this illness, and one of the ways we can do so is through genetic testing – although it has been a controversial subject recently, it can help us decide which routes of treatment may be most beneficial in helping them recover –we now have more evidence that by identifying individuals who are carriers of the methionine polymorphism, it may be more effective to treat them with methods like exercise, which they are more responsive to. Valine carriers may not respond as well to exercise, which informs us that perhaps alternative routes are required to treat these individuals if they are diagnosed with depression. Assessing this could provide patients with more personalized, precise treatment options that would greatly aid their recovery efforts.

Low-Intensity Training

While HIIT does seem perfect for younger patients, and a younger population in general, it may not be applicable for older individuals or those with injuries. For these individuals, the literature does seem to support the benefits of lower intensity exercises like yoga and meditation. For example, Bonura et al.'s findings in their 2009 review established that yoga can also serve as a strong therapeutic agent for older populations, revealing it to be more effective at reducing stress than chair aerobics or even walking.[221] As many of the individuals who the researchers studied had suffered from arthritis or other ailments, yoga proved to be the preferred form of activity for the cohort. Therefore, as we get older or accumulate injuries, it seems perhaps more useful to shift to yoga or meditation as a preferred form of therapy, as it is less stressful and more accessible, physically, for most individuals.

A 2015 study reinforced this idea by finding that for middle-aged women who were suffering from depression, finding the time to walk for about 200 minutes each week was correlated with better emotional health, increased energy, and greater socialization.[222] These results were found both immediately after the study as well as during a follow-up three years after it, although this follow up improvement was not as large, which still drives home the importance of consistency. An important point to consider is that the results found in the subjects who were requested to walk 200 minutes paralleled the results found in women who were asked to complete 150 minutes of moderate-intensity activity every week. When applying this to the general population, we must therefore ensure that the frequency of exercises like walking can make up for its lowered intensity. This also drives home our earlier point that perhaps the benefits of exercise are dependent on relative exertion, which would further bolster the argument for HIIT training. For many older adults, this would mean more time would have to be spent taking care of their health than younger individuals, which is something that therapists and public health officials need to take into account when caring for aging populations.

However, even healthy and active individuals can, and should, be encouraged to invest extra time to add yoga, tai chi, or meditation to their fitness routines. Alderman et al. demonstrated promising results by asking subjects to complete a half hour session of focused-attention meditation, immediately followed by another half hour session of aerobic exercise, twice a week for eight weeks.[223] Focused-attention meditation requires its participants to focus on their breathing, and in doing so, direct their thoughts away from their past or future, to prevent rumination. Also called mental and physical (MAP) training, this technique has been promoted as an effective substitute to conventional methods of depression treatments, particularly antidepressants. Citing the neurogenesis hypothesis of depression, this study claims that MAP training is useful because it not only requires subjects to expend considerable mental energy to learn a new technique and apply it consistently, its required physical training also promotes neurogenesis through the proliferation of BDNF, which has been discussed earlier in this paper. And as a result of this training, the study found that all of the 52 subjects tested reported alleviated symptoms of depression, and spent less time ruminating as well. Indeed, multiple meta-analyses of the impact of yoga on a variety of mental health measurements studies recommended it as a tool to decrease symptoms of anxiety and depression.[224, 225, 226]

A point to note is that many studies have found that depression is more common and severe in younger populations than in older ones, although this trend picks back up when individuals reach extremely high ages.[227, 228] In addition, psychological studies have shown that

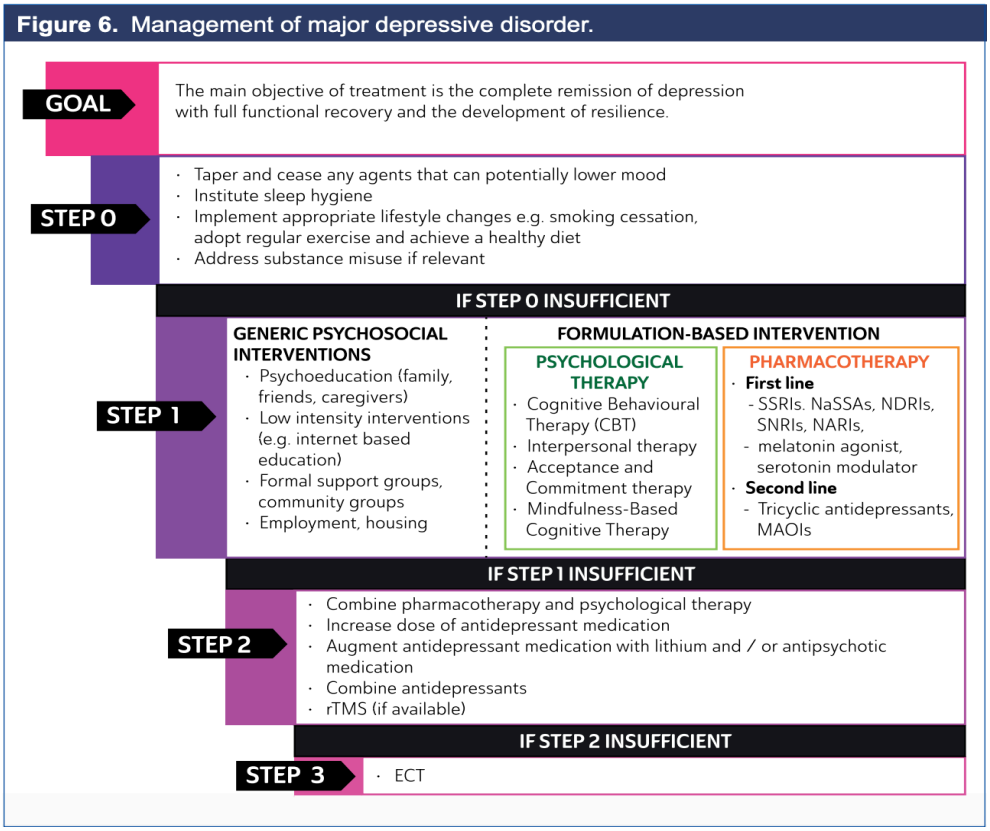
emotional stability tends to increase with age, which further lends support to the trends mentioned above.[229, 230, 231] Referencing my earlier point that the vigorousness of exercise is positively correlated with better outcomes for severely depressed individuals, I believe that this further supports the use of lower intensity exercises for older populations. In contrast, for college-students and younger patients, we can take advantage of their youth by asking them to complete more intensive training. This can provide for greater benefits, especially during their formative years, where they may have weaker emotional regulation and may be more susceptible to greater mood swings.

In summary, aerobic exercise tends to be more effective than resistance training in aiding individuals with depression. Although resistance training does seem to aid depressive symptoms, it plays a far greater role in alleviating anxiety symptoms, and so should not be ignored here. One of the primary factors in this discrepancy in treating depression may simply be the fact that aerobic training more directly leads to increased blood flow to the brain. And in this case, HIIT can provide the best of both worlds for most individuals, as we can use it to pair the intensity, muscular fatigue, and testosterone production of resistance training with the cardiovascular benefits of aerobic exercises. However, for older adults, or for individuals with disabilities, low-intensity training such as yoga or meditation might be preferred. With this conclusion in mind, I'd like to use the work covered in my thesis to propose how college students and the general public can utilize the specific exercise patterns covered to improve their mental health.

CHAPTER 3: APPLICATIONS

Let's start by taking a look at how depression is typically treated in the US. If we reference the guidelines set by the American Psychiatric Association, we find that antidepressants and therapeutic options tend to be the recommended first line of treatments. In the APA's Quick Reference Guide to treating depression, the word "exercise" is mentioned twice – once in relation to promoting "healthy behaviors such as exercise, good sleep hygiene, [and] good nutrition," and again in relation to helping manage weight gain, a potential side effect of certain antidepressants, with the full sentence reading "Encourage exercise."[232] The National Institute for Mental Health reflects a similar, albeit slightly different attitude towards utilizing exercise for depression, instead listing it under the heading "Beyond Treatment: Things You Can Do."[233] This categorization fails to legitimize exercise as a proven method of treatment that, for mild to moderate cases of depression, is on par with antidepressants and various methods of therapy. By separating it from these other methods, it neglects the possibility of combining these options, and distances exercise from the possibility of being a useful tool that medical professionals can use to treat their patients. It also fails to realize that for many individuals with depression, exercising requires significantly more motivation and effort than taking a pill, or even attending a therapist-led counseling session. The suggestion that patients must take the initiative here, rather than their counselor or physician, may confuse or overwhelm those who simply don't have the same clinical knowledge as professionals to craft an effective plan for their improvement.

Many other developed countries take a different approach, however. For example, the United Kingdom views exercise as a first-line treatment, along with antidepressants and therapy, for mild and moderate cases.[234] And down under, the Royal Australian and New Zealand College of Psychiatrists first determines if patients can be treated with exercise successfully, before considering medication and therapy.[235]



Attached above is a diagram from their recommendations that places exercise at "Step 0," to be considered before conventional treatment options, which are placed at "Step 1."

Part of the reason for this discrepancy is due to the differences in these countries' healthcare systems. Countries like New Zealand and Canada, which have single-payer systems, are incentivized to support low-cost, proven options first, before moving on to more expensive treatments.[236, 237] Most citizens in the US do not have this luxury, and this has created a system that incentivizes profits. Because insurance providers reimburse psychiatrists for each appointment they create, it's simply easier and faster for them to write their patients a prescription for a medication in the little time they have together. Not only does this provide the patient with a quick fix for their symptoms, physicians can also fit in more patients in a day. This is evidenced by the more than 400% rise in antidepressant use since 1988, which has now made them the third most prescribed class of drugs in the nation, behind only painkillers and cholesterol medications.[238239]

For many psychiatrists, this has become less of problem, as currently only about 55% accept insurance, the lowest number of any medical specialty, in order to ensure higher quality visits with their patients.[240] However, most of the patients who are prescribed antidepressants don't see a psychiatrist first – 62% of prescriptions are actually written by general practitioners, pediatricians, or OB-GYN's, and 73% of these patients are not even diagnosed with a particular illness before they receive their prescriptions.[241] It's extremely common for physicians to prescribe antidepressants to help their patients deal with conditions like insomnia or chronic pain, of which depression is often a side effect. But in these cases, offering temporary relief doesn't do much to help the root cause of their patients' problems.

This leads us to another problem – there is a cultural divide in the way we view exercise. Only 23.5% of American adults get enough of the recommended aerobic and resistance exercise that is suggested by the US Department of Health and Human Services.[242] Close to two-thirds of Americans are overweight, and more than one-third are obese.[243] When these markers of the general population were compared to rates among physicians, the doctors did not fare as well as we would hope. 30% of physicians reported exercising less than once per week, and almost half of them reported that they wanted to lose weight.[244] It is not surprising, then, to find that these habits are rarely emphasized during their training, as only 6% of medical colleges require medical students to take a class on physical activity and exercise.[245] Because of this, many general providers feel that they aren't trained adequately to use this route in treating their patients, and it clearly shows in the way they practice. Only 40% of patients who informed their primary care physicians that they were experiencing depressive symptoms were told to try exercising.[246] The solutions that we can offer for therapists and mental health professionals here may be applicable to most physicians as well.

Suggestions for Medical Professionals

With the evidence provided above, I believe that high intensity interval training may provide the greatest overall advantages for mental health patients and the general public, especially younger individuals. Firstly, its greater intensity will require individuals to push themselves much harder in a given time span than if they were only completing moderate-intensity endurance training or resistance training. Namely, the routine's increased blood flow to the brain, and its resulting increase in the synthesis and release of key proteins and hormones may provide those who are experiencing more severe symptoms of depression with the greatest

overall improvement as compared to other forms of exercise.[247, 248] On top of this, its shorter duration means that it can be more easily added to a busy individual's schedule, since moderate-intensity exercises require longer periods of time to reach the target heart rate that interval training can provide its users.[249] Finally, HIIT has a high degree of programming variability, which allows it to be modified to fit patients from virtually all walks of life.[250] It can be modified around weight-training, as is being popularized by CrossFit, it can be programmed around sprint and plyometric training, as is often being done for athletes looking to gain explosiveness and power, and it is intrinsic to sports that revolve around short bursts of speed and strength, like football or basketball. In addition, for individuals who are suffering from anxiety, HIIT training is well known for its ability to facilitate muscle growth and boost testosterone levels in its users, which was one of the primary reasons why resistance training had such a profound impact on individuals with symptoms of anxiety.[251] This means that individuals who program their HIIT regimen correctly can reap the cognitive benefits of both steady-state cardio and weight training.

With all this being said, it's important to note that HIIT is, by definition, high intensity, and I do understand that many individuals across all ages may not have the pre-existing health, activity level, or even motivation, to complete such challenging workouts. HIIT training would be inappropriate for older populations, who may see a significant increase in the risk of injury or fatigue.[252] The same can be said for younger individuals who are not as healthy as many of their peers. However, to deal with this issue, the high degree of variability involved in HIIT comes into play, as individuals can program workouts that are low impact and may be easier on their joints, through routines involving swimming or cycling.[253]

Another problem with this type of training is that it may not be appealing for individuals who are struggling to attain the motivation to ease into a healthier lifestyle. HIIT would be akin to teaching someone how to swim by throwing him or her into the deep end of the pool. It is somewhat like the drill-sergeant of workouts – while this may be ideal motivation for some people, unfortunately many individuals do not respond well to this type of incentive. Instead, they are much more likely to experience even more negative or self-defeatist thoughts, and quit such intense programs early on.[254] It's important then, to reach out to these individuals and help them get started with a training plan that will ease them into higher intensity workouts as their health and fitness improves. Each individual's perceived level of exertion is different – what one individual feels is a moderate-intensity exercise may seem instead like a very high-intensity exercise for someone else. In this case, we can start individuals out with lower intensity exercises like tai chi, yoga, or walking. Once the individual feels comfortable completing these exercises, we can gradually warm them up to the idea of pushing themselves just a little bit further each week.[255] And this level of progression would continue, with the workout's intensity paralleling the individual's motivation to start their workout. If individuals feel that this level of progression may be too slow of a pace for them, they can program around the suggested pace to fit their level of comfort.

We can look to psychiatrist Madhukar Trivedi, at Southwestern Medical Center, for advice on how therapists can set up plans for their patients. In formulating treatment options, he first ensures that his patients are aware of all of the treatments available to them. Patients tend to be so focused on antidepressants, for the reasons stated above, that they may not be aware of more effective options for their specific circumstances. If he feels that a patient would benefit from exercise, he works with him or her to plan a weekly workout schedule that best fits his or her needs.[256] While this is a solid start, Dr. Trivedi has stated concerns regarding his patients'

ability to adhere to these regimens.[257] In order to increase patient compliance, I would propose asking patients to track their workouts using apps like MyFitnessPal or Fitbit, and then showing their therapist their progress during scheduled counseling sessions. In this way, it would provide both parties quantitative data regarding the patient's improvement, and would serve to hold the patient accountable as well. At each visit, they can monitor their progress and re-evaluate and set new goals to achieve for the following week. And this consistent re-evaluation can also prevent the patient from relapsing into previous sedentary behavior. More importantly, if patients are not able to go to the gym consistently, professionals can determine if there are other factors holding the patient back - perhaps they are struggling with the motivation to enter the gym, or they may not have access to such facilities. If motivation is the issue, then perhaps this can be one of the focal points of their therapy sessions, to provide enough encouragement to get the patient out of bed and into the gym in the first place. I know all too well the feeling of being intimidated when I walk into the gym and see people who seem to be much healthier and happier than me. If this is the primary factor behind someone's reluctance to work out in a public gym, perhaps we can ask them to work out at home with simple body weight exercises with low rest times, to help them both get their heart rate up and complete lower intensity training that can help them become comfortable with their bodies. This solution would encourage greater communication between the pair, allow more flexibility in crafting a plan tailored to the patient's needs, and strengthen the patient's relationship with his or her therapist.[258]

So, what should such a specific plan look like? For most individuals, 150 to 300 minutes of moderate intensity physical activity is recommended.[259] As most people spend about 7.7 hours per day being sedentary, cutting this number down by just one hour per day is substantial in helping improve Americans' health.[260] One way to help track progress here would be through measuring the number of steps individuals take each day. 10,000 steps per day is the ideal number to shoot for, as recommended by the Department of Health and Human Services.[261] Even if individuals don't exactly hit this number, it is much higher than the current average of 5000 steps that most Americans take daily, and will be enough of an increase to make a significant difference in their well being.[262]

When it comes to depressed patients, then, it would be recommended to exercise three to five times per week, according to Dr. Trivedi, and in order to ensure adequate intensity, each session should last for at least 45 minutes.[263] Patients should also aim to reach close to 80% of their target heart rate during aerobic exercise sessions. Two psychiatrists, Dr. Jasper Smits and Dr. Michael Otto, have created a manual to aid psychiatrists, called "Exercise for Mood and Anxiety Disorders, " and their suggestions parallel Dr. Trivedi's. They have suggested getting between 30 to 60 minutes of moderate exercise about five times per week, or getting about 20 to 60 minutes of intense exercise about three times per week. They elaborated on this further, suggesting about two days of resistance training and two days of aerobic exercise per week.[264]

Guidelines from a 2010 conference held by the Anxiety Disorder of America also offer the idea of a "prescription card," which lists the frequency, intensity, and amount of exercise each patient is to complete, along with his or her level of experience, level of confidence, and current level of motivation to complete the training.[265] With a basic framework like this set, therapists can then feel free to work with their patients to personalize this plan according to their client's preferences, pre-existing conditions, and level of comfort and interest in certain exercises. And every week, with the patient's permission, an exercise of a higher intensity could be added on to allow the patient to continually improve.

To help track their progress, patients could use apps like MyFitnessPal or Fitbit to obtain readings of data like their heart rate, steps taken, and calories burned during the workout session. Measuring the number of calories lost during the session would also be a simple way of ensuring that the patient's workout met the targeted intensity level. However, since caloric output is also dependent on other factors like diet, this would have to be individualized for the patient and his or her goals. Losing a higher number of calories in a shorter time span would be expected from more intense sessions, while a lower number, or a longer time span required to lose a certain number of calories, would be associated with less intense sessions.[266] Here it is important to note that resistance training would be a special case, since it burns a smaller number of calories as compared to aerobic training during the workout session, but is much more metabolically expensive the day after the workout, as the body continues to recover – patients requiring resistance training would have a smaller initial calorie threshold, which would also prevent excessive delayed onset muscle soreness, or DOMS, that could hinder beginners from returning to that workout in the future.[267]

Ideally, this plan would be combined with another form of treatment, such as antidepressants or therapy, as research states that the recovery rate for patients using a single treatment option is 50%, but the recovery rate for those adding one more rises to 70-80%.[268]

What is most important here is that the therapist provides structured and explicit guidance to his or her patients. Simply telling them to go to the gym is not going to be enough. A statement like this does not imply that exercising is a significant part of the patient's treatment, and moreover, does not provide the patient with enough information for them to feel as if what they are doing has an explicit purpose. Patients who hear this will not prioritize exercise, nor will they be consistent in utilizing it.[269] Vague instructions can also pose other issues for certain populations for patients. For example, older individuals struggling with depression may not be as aware of the gyms or fitness centers around the community, and may need extra guidance in navigating the Internet to search for one nearby.[270]

One of the keys to achieving compliance is to promote exercising with a measurable goal in mind – ultimately, one of the best ways to stick to a workout plan is to focus on the end result of that plan. For example, a patient who has started working out can perhaps focus on losing a few pounds of bodyweight, or reducing their mile time by one minute in about two months. By diverting their attention from the problem at hand, namely their mood disorder, they can ultimately focus on achievement in a separate field. Not only will this get their mind off of their mental health, but being able to see progress can help them stay motivated throughout the process, and the feeling of accomplishment can work wonders for their self-esteem.

On top of this, since many patients may feel that they must rely on their therapist for help, prescribing an exercise plan gives the patient the chance to take back control over their lives. It can help them become more comfortable with the responsibility of taking care of themselves, and can reduce feelings of helpless, which is one of the key markers of depressive and anxiety disorders.[271] By being able to change such a habit at this stage, we can ultimately provide patients with the keys to being able to confront their issues independently, and become empowered to take proactive steps to improve their lives. And it is here that we can see the biggest impact of exercise – individuals can take ownership of their health, and make exercise and self-care a habit for themselves, which is the ultimate goal of my thesis.

Attached below is a sample plan that a therapist could create for his or her patient:

WEEK 1

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
Morning	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)
Afternoon		Therapy		Therapy			
Evening	**Weightlifting (45 min)**		**Cardio (60 min)**		**Weightlifting (45 min)**	**Cardio (30 min)**	
	• Quads: Leg Extensions		• Track: Walk 1 mile + Jog .25 miles (Repeat 3X)		• Quads: Leg Extensions	• Track: Walk 1 mile + Jog .25 miles (Repeat 3X)	
	• Glutes: Glute Kickbacks		• Stationary Bike: Cycle 3 miles.		• Glutes: Glute Kickbacks	• Stationary Bike: Sprint 1 min	
	• Hamstrings: Hamstring Curls		• Stationary Bike: Sprint 1 min		• Hamstrings: Hamstring Curls		
	• Back: Lat Pulldown				• Back: Lat Pull-down		
	• Chest: Chest Fly				• Chest: Chest Fly		
	• Shoulders: Shoulder Press				• Shoulders: Shoulder Press		
	• Abs: Crunches				• Abs: Crunches		

WEEK 2

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
Morning	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)	Zoloft (100 mg)
Afternoon		Therapy		Therapy			
Evening	**Weightlifting (45 min)**		**Cardio (60 min)**		**Weightlifting (45 min)**	**Cardio (30 min)**	
	• Quads: Leg Extensions		• Track: Walk .75 miles and jog .25 miles (Repeat 3X)		• Quads: Leg Extensions	• Track: Walk .75 miles and jog .25 miles (Repeat 3X)	
	• Glutes: Glute Kickbacks		• Stationary Bike: Cycle 3 miles.		• Glutes: Glute Kickbacks	• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 2X)	
	• Hamstrings: Hamstring Curls		• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 2X)		• Hamstrings: Hamstring Curls		
	• Back: Lat Pulldown				• Back: Lat Pull-down		
	• Chest: Chest Fly				• Chest: Chest Fly		
	• Shoulders: Shoulder Press				• Shoulders: Shoulder Press		
	• Abs: Crunches				• Abs: Crunches		

WEEK 3

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
Morning	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)
Afternoon		Therapy		Therapy			
Evening	**Weightlifting (45 min)**		**Cardio (60 min)**		**Weightlifting (45 min)**	**Cardio (30 min)**	
	• Quads: Leg Extensions		• Track: Walk .75 miles and jog .25 miles (Repeat 4X)		• Quads: Leg Extensions	• Track: Walk .75 miles and jog .25 miles (Repeat 4X)	
	• Glutes: Glute Kickbacks		• Stationary Bike: Cycle 3 miles.		• Glutes: Glute Kickbacks	• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 3X)	
	• Hamstrings: Hamstring Curls		• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 3X)		• Hamstrings: Hamstring Curls		
	• Back: Lat Pulldown				• Back: Lat Pull-down		
	• Chest: Chest Fly				• Chest: Chest Fly		
	• Shoulders: Shoulder Press				• Shoulders: Shoulder Press		
	• Abs: Crunches				• Abs: Crunches		

WEEK 4

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	SUNDAY
Morning	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)	Zoloft (90 mg)
Afternoon		Therapy		Therapy			
Evening	**Weightlifting (45 min)**		**Cardio (60 min)**		**Weightlifting (45 min)**	**Cardio (30 min)**	
	• Quads: Leg Extensions		• Track: Walk .5 miles and jog .5 miles (Repeat 3X)		• Quads: Leg Extensions	• Track: Walk .5 miles and jog .5 miles (Repeat 3X)	
	• Glutes: Glute Kickbacks		• Stationary Bike: Cycle 3 miles.		• Glutes: Glute Kickbacks	• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 4X)	
	• Hamstrings: Hamstring Curls		• Stationary Bike: Sprint 1 min + Rest 1 min (Repeat 4X)		• Hamstrings: Hamstring Curls		
	• Back: Lat Pulldown				• Back: Lat Pull-down		
	• Chest: Chest Fly				• Chest: Chest Fly		
	• Shoulders: Shoulder Press				• Shoulders: Shoulder Press		
	• Abs: Crunches				• Abs: Crunches		

One counterpoint to these suggestions is the argument that keeping track of this much information may be too much for therapists to handle. Do therapists have enough knowledge of exercise to put together a well-structured "prescription?" This is a legitimate concern, and it is one that must be addressed at every level of psychology. It is my hope that placing a greater emphasis on exercise as a form of psychiatric therapy will allow the medical community at large to start considering exercise itself as a form of medicine. With this shift in focus, perhaps this could allow more research to be conducted into the differences between the specific types of exercises, and how they can be utilized to treat a wider range of ailments. The discoveries made as a result of this research could allow mental health facilities to place more importance on exercise as a tool for future professionals to use. This, in turn, would allow for greater precision in prescribing it to patients in the future.

While this does not reflect reality currently, there are still many options for mental health professionals to ensure their patients get the care they deserve. For example, patients who need to undergo physical rehabilitation get help from physical therapists, who craft a careful guide of stretches and movement patterns for their patients.[272] For mental health professionals, partnering with personal trainers may be useful for therapists who want their patients to exercise, but are unsure of where to start. Personal trainers and coaches, who have more extensive knowledge in this area, can help therapists and their patients craft a solid plan while considering factors such as the number of workouts required per week, the intensity of the workouts, the patient's previous level of experience, and their short-term and long-term goals. Even if this is for the first few appointments only, this may help increase motivation in certain patients, and can help them establish the habit of going to the gym consistently. It also provides patients with another supportive individual they can turn to for guidance, especially at a time when they are at their most vulnerable. Another avenue is to partner with public, community gyms to allow patients to perhaps receive discounted monthly fees for signing up and consistently showing up.

One idea that I am a bit hesitant to propose is the idea of a therapist setting up a buddy system between two or more of his or her patients. If he or she believes that certain patients may have similar issues or experience levels, he or she can ask his or her patients if they feel comfortable partnering up with another patient over the coming months. This could alleviate any issues regarding motivation that these individuals may be facing; however, I do understand that this may not be as popular of an idea for some patients. Many individuals may feel that this diminishes key aspects of the provider-client relationship, including privacy, and could lead to a less intimate, personalized approach to therapy.[273] Still, it should not be ignored entirely, as some patients may opt for it, citing the increased social support it may provide as a net positive of the approach.

Suggestions for Communities

Outside of the doctor's office, we must explore ways to implement exercise into public health in order to ensure that the community at large is active. The easiest way to do this is to ensure that people start these habits at a young age. It's especially important to promote exercise in school, where it can have some of its most protective effects on young children. However, many schools have designated less and less time for recess. After the federal No Child Left Behind Policy shifted schools' focus to standardized test scores, many struggling schools opted to dispose of recess, as they started to believe that more time needed to be spent preparing for these exams. The center on Education Policy reports that between 2001 and 2006, 20% of

schools reduced the time that children had for recess.[274] Worse, by the end of that year, the study found that a staggering 33% of elementary schools did not offer daily recess for any of their students.[275]

The National PTA is just one of many organizations around the country that is lobbying for legislation that will allow children to spend more time playing with each other outside the classroom.[276] As of last year, five states had laws protecting a 20 minute recess for elementary school children, and seven more mandated that children be afforded around 30 minutes of physical activity daily, with more states trying to push that number closer to an hour.[277] But the number of states pushing for such legislation is still far too small. One criticism that has been cited is the fear that too much time for recess would eat into the children's already busy schedules.[278] To help navigate these issues, perhaps it would be useful to look into less traditional solutions. For example, some school districts in Texas have provided their children with four 15 minute periods of recess between classes, which not only meets national recommendations, but may provide more flexibility for teachers and schools.[279]

However, I believe that these guidelines should not stop with elementary school children. Middle schoolers and high schoolers receive much less time for recess or free time than elementary school children.[280] Yet at a time when students are starting to become more and more challenged academically, wouldn't it make sense to ensure that they are given time to alleviate this stress? Recess is often replaced at these levels by physical education classes, which are supposed to provide a more focused, educational approach to physical fitness for teenagers. However, the median budget for physical education across American schools is $764 per year, a number that is pitiful compared to the $12,000 that accounts for the medial total annual expenditures per pupil.[281] Of course, these budget cuts hit schools in urban areas much harder than suburban schools, and this effect is associated with much lower test scores and academic performances in these regions as compared to schools in the rest of the country.[282] Unfortunately, this issue is something that can primarily be solved through lobbying for effective legislation, which would allow for more funding to be funneled into these critical areas.

In areas where legislation has stalled, I propose that schools could take matters into their own hands. For example, perhaps schools can track not only students' grades, but also their health, to ensure that students are showing improvements in their screenings. This way, any students who may be struggling academically can first have their overall physical health examined as a possible cause of their troubles. These students could then be given special attention by school officials, so that they are provided with increased time for exercise, or reduced-calorie school lunches to help manage their health. Essentially, this "physical tutoring" would be akin to academic tutoring in that students who are at a higher risk of complications can be more quickly directed to the resources they'd need to help them recover. In this way, schools would demonstrate that their children's physical well-being is just as important to them as their grades, without placing excess pressure on students.

In Massachusetts, some schools have asked patients to become more involved in before and after-school programs, which also has helped take some burden off of teachers and staff in providing supervision for these children.[283] Parent volunteers lead hour-long sessions before and after school that allow children to play games like tag and Frisbee. This program, known as Build Our Kids' Success, or BOKS, has been adopted at close to 3000 schools around the world.[284] A Harvard study that analyzed the impact of this program found that while it did not

reduce children's body mass indexes over a 12 week period, children who participated in the program reported that they looked forward to attending the programs each day, and felt that they had grown closer to their friends at school.[285]

Schools that may not be able to provide these resources for their children can still try to boost activity by encouraging their kids to walk to school. The California Department of Public Health has made a concerted effort to provide safer routes to school for children, so that they can fit in a few more minutes of activity each day.[286, 287] Providing these routes also helped parents feel more comfortable with walking with their kids to school, and even letting the children walk with friends if the school was close by. This emphasis on providing adequate walking paths is an important point that we will revisit soon, as it applies to the field of urban planning and development.

After grade school, many students opt to attend college, where they often get to choose their own schedule and methods of learning. As of 2010, only 39% of colleges required their students to take physical education classes as part of their core curriculum. This is in stark contrast to the 1920's and 1930's, when about 97% of colleges mandated that physical fitness be taught alongside core subjects.[288] Much of the reasoning behind this was the fact that most colleges were predominantly male at the time, and were concerned about preparing young men to be able to fight in the military amidst increasing international tensions. Today, fortunately, the demographics have shifted significantly and we have vastly different reasons for encouraging physical fitness. Given what we've learned about the impact of exercise on mental health, doesn't it make sense to have colleges start requiring physical education classes again?

Several universities can serve as models for us to start with. For example, Massachusetts Institute of Technology requires that every able-bodied student take four six-week physical education classes by the time they complete their degree.[289, 290] Spelman College requires its students to complete 15 hours of PE to graduate, allowing them to choose between a wide range of courses and sports.[291] Prestigious institutions like Columbia University and Wellesley College have done the same.[292, 293] And Oral Roberts University encourages its students to wear Fitbit watches to track their wellness, and has set up a unique rewards system based on their progress.[294]

I would like to push these requirements further, and propose that all able-bodied students at a four-year college be required to take one physical fitness class of their choice per year in order to maintain good standing and be eligible to graduate. Of course, if students have a physical disability that prevents them from doing so, or are concurrently involved in an athletic program, they would be exempt from this requirement. Usually, these classes tend to meet about three times a week, and have very few assignments outside of class, which not only allows students to meet the recommended guidelines for physical activity each week, but also provides them with course credit for little extra stress or work.[295] On top of receiving academic credit for taking care of their health, these classes can help them learn how to work out effectively and safely, and can ultimately help them set up long term habits that will ensure that they can take care of their health in the future. If students aren't comfortable with required exercise, perhaps universities and colleges can set up buddy systems to help classmates meet other students who are interested in exercising and working out together, to hold each other accountable each week as well.[296]

One argument against this idea could be that this policy could raise problems such as body shaming, or even obsessive thoughts that could precede eating disorders or body dysmorphia.[297, 298] As these criticisms are indeed legitimate, I would argue for very broad requirements that allow students the freedom to pick classes that they are interested in, and ensure that the focus of these classes be on participation rather than on competition that encourages unhealthy comparisons between students. In this way, these classes would only be focused on ensuring that students are making an effort to take care of their general physical and mental health. UT Austin currently offers 34 classes in physical education across twelve sports and activities, which ensures that all students have the freedom to choose the classes they'd like.[299] Below is an excerpt from the syllabus of UT Austin's Cardiovascular Weight Training class, which demonstrates both its relaxed requirements and its primary emphasis on consistent physical activity. The course only requires students to bring a notebook and pencil to class to log their workouts, and the final grade is determined mostly by the students' attendance:

Cardiovascular Weight Training PED 106C – 12160 Spring 2019

Time:	MW 8-9:30 am
Instructor of Record:	Nicole McLagan, nmclagan@utexas.edu
Instructor:	Joey Dragonette
Office:	N/A
Office Hours:	By appointment
Classroom:	RSC 1.136 (Weight Room)
E-mail:	jedragon@utexas.edu

Course Description: Course is designed to enhance basic knowledge of exercise with respect to both aerobic and anaerobic systems. Students will learn skills associated with these and utilize them each class period. Additional topics to be covered include the principles and benefits of physical activity and the relationship between exercise, health, and wellness. Students will learn the components of a safe fitness program and basic training principles for both cardiovascular training and weight lifting. Students will be able to demonstrate skills of training including warm-ups, stretches, various exercises, and cool-downs.

Goals/Objectives:

1. To develop an understanding of fitness principles that will be applied to workouts both during class and outside class
2. To recognize and engage in a variety of exercises to improve cardiovascular & muscular strength and endurance
3. To enable students to set and reach personal fitness goals

Required Materials:
A small, bound notebook. Students are required to log and record all workouts. Students will be taught how to properly record sets and reps in their logs. Students will turn in logs at the end of the semester, so I recommend that you do not share this notebook with any other class. Students should bring this along with a pen or pencil to record workouts and/or take notes.

Mid Semester Check: Submit via canvas a paragraph on your improvements in Fitness and anything that you would like to see implemented in to your class. Things you'd like to learn about, different workouts, favorite workouts you want to do again, etc.

Grading Policy:

Attendance/Workout Completion	**85**
Workout Log	**10**
Mid Semester Check	**5**
Total	**100**

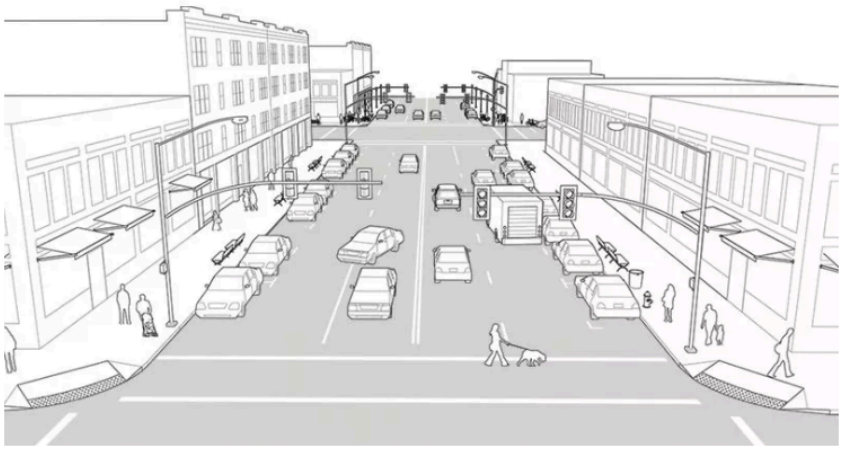
Another argument that can be used against this idea is the fact that many students spend considerable time walking to class, and that this level of daily activity is sufficient. While this is a great option for an older population, we have seen in the previous chapters that walking is simply not vigorous enough of an activity for a population as young as college students. Walking, by itself, especially at such young ages, is not active enough to promote these protective effects and habits later on in life.[300] I also believe that this requirement is especially important for students who are taking online classes, and do not spend as much time walking as those taking courses involving face-to-face interaction with their professors.[301] One way to deal with this issue is to limit the number of online classes students can take if they attend that campus, so that they are required to move around to a greater extent. Alternatively, universities could require that after signing up for a certain number of online classes, students must take an additional exercise class per year to ensure that they are staying active.

An idea like this may spread to other aspects of students' lives, and may encourage a more complete view of wellness from students. For example, Dr. Michael Scullin of Baylor University offered extra credit to students if they wore a sleep tracker during the week of their final exams and proved that they received at least 8 hours of sleep each night. 8 students accepted his challenge the first time he offered it, and they slept for an average of 9.17 hours per night, as compared to the students who did take the challenge, who finished with 6.36 hours of sleep per night. The second time he offered the challenge, under different conditions, he found that 87.5% of the students who accepted the challenge improved on their baseline sleep duration. Many students commented that they felt much more refreshed throughout that week after having accepted his challenge.[302] When he analyzed the impact of this study on his students grades, the students who received more than 8 hours of sleep every night performed better on their final exam than they had in the class prior to finals week, with a z-score of about .2. The group that slept less actually scored worse on their final than their grade in the class, with a z-score of about -.2. It is clear that a greater focus on overall wellness through such tracking can promote academic success and mental health, and I strongly urge more colleges to take up such incentives to help their students succeed.

If children and teenagers can benefit from more activity at school, then adults are sure to benefit from more activity at work as well. Lately more and more companies are looking for ways to promote employee health. Companies in Louisiana have started well-ahead programs that have helped encourage and support organizations that promoted healthier habits and workplace wellness programs. Some of the ideas used included replacing junk food in vending machines with healthier, lower-calorie snacks, and company-wide initiatives to reward employees who took the most steps per month.[303, 304] Another possible suggestion here might be to try to shut down most elevators once every week, to encourage employees to take the stairs more often. One or two elevators could be reserved for individuals with disabilities, as well as freight elevators to move heavy equipment between floors. An alternative to this could be to encourage guided, daily ten minute stretching or meditation sessions that employees could complete together.[305, 306] Another potential promotion could be incentivizing non-monetary prizes to employees who choose to bike to work instead of driving. An event like this could be facilitated simply by adding more bike racks to the company parking lot, to encourage employees to expend a few extra calories on their way to work.[307, 308]

According to the Community Preventive Services Task Force, there are many strategies that neighborhoods can employ in order to promote physical activity among their residents.

Returning to our earlier point about walking trails, one of the most important methods is through urban design and zoning policies.[309] By creating more areas for people to practice walking safely, communities can not only increase areas in which residents can play organized sports or ride their bikes, but also provide scenic routes for people of all ages to take walks through their neighborhoods. This relatively unique aspect of urban design is known as "walkability," or how easy it is to complete errands around the city without a car.[310] Crowded metropolitan areas like New York, Boston, and Austin have higher walkability scores than rural areas, which promotes a greater amount of physical activity among their citizens.[311] City planners should be incentivized to allocate a greater proportion of the city's land to creating public spaces like sidewalks and green areas like parks and gardens. Hamburg, Germany, is leading the way in this endeavor through its Green Network Plan, which has helped it cover almost 40% of its city with walkable spaces.[312] Below is an illustration from the National Association of City Transportation that shows a few simple changes to add to a city intersection to promote the walkability initiative:



The National Association of City Transportation provides before and after blue prints of what an auto-oriented street would look like if transformed into a people-oriented street. | National Association of City Transportation

The benefits of such an intervention would especially be seen in crowded cities – individuals living here would essentially be able to bring the gym to themselves, as they could go for a walk, jog, or bike ride much more conveniently. Policymakers could follow the lead of certain states that have expanded upon these innovations. For example, the Arkansas Bicycle and Pedestrian Transportation Plan set forth an expansion of the state's sidewalks, and created more bike lanes along its roads.[313] It also created a statewide bikeway network that established new trails connecting frequently visited locations, allowing more citizens to bike or walk safely between their destinations, an initiative also emulated by Utah.[314] Up north, cities in Michigan have passed zoning amendments that have required bike parking to be added to newly constructed buildings, to promote cycling as a convenient method of transportation for its residents.[315] And from an economic standpoint, the children who are unfortunately most affected by these problems are those in impoverished neighborhoods. Since walkability inherently allows for greater ease of access in locations with the highest population density, designing communities with these goals in mind would be ideal. Although it is much easier said than done, sister communities could implement shared-use policies that would very much come to the aid of poorer districts that may be in greater need of these solutions.

Importantly, one of the most straightforward approaches to increasing community access to exercise could be to just focus on gyms and fitness centers, by working to make them more affordable for taxpaying citizens. One approach could be to allocate a greater portion of taxes to the funding of community gyms, which could cut down greatly on the membership fees that citizens would have to pay each month. Perhaps by having higher earning citizens foot a greater percent of the bill, individuals in a lower socioeconomic status, and those who may need exercise the most, may now be able to enjoy greater access to such community goods. Essentially, this would allow community gyms to function in a manner fiscally similar to the community library. One example of this is Healthworks, a nonprofit gym in Boston that charges no more than $30 per month, with its membership fees being determined based on its clients' income levels.[316]

More than this, many urban areas share their already crowded neighborhood with large sports stadiums, most of which have been heavily funded by taxpayers. As these arenas have top of the line gyms and wellness facilities, it could be a good idea to allow taxpayers access to these amenities during certain hours of the week. 36 of the 45 major sports stadiums that have been built since 2000 have paid for in part by their respective cities' taxpayers.[317] These bills have amounted to a cost of over $3.2 billion for their citizens, who, on average, foot about 40 to 50% of the bill.[318] It seems only fair that taxpayers are allowed to use what they've helped pay for. These organizations and communities could also focus on promoting sponsorships from corporations to increase youth sports participation. For policymakers, this is relevant because when dealing with a tight budget, reaching out to certain corporations to sponsor youth programs and tournaments could be very fiscally responsible. The aforementioned BOKS program, sponsored by sports giant Reebok, has seen great success in communities at home and abroad, and can serve as a model for similar initiatives to emulate.

Suggestions for the Media

In an increasingly connected population, any campaign to increase fitness would be served well by using social media platforms as tools. When polled, most people have reported that social media served as an overall a positive force in their lives, as they feel it both connects people to each other, and keeps them in the loop about current events.[319, 320] For example, the ALS ice-bucket challenge was one of the most successful campaigns in recent memory, with the ALS Association encouraging participants to pour ice-water over themselves to promote awareness of the disease. In 2015, the Association reported that over 3 million people had donated a total of more than $100 million to their campaign, most of which went to furthering research into the disease.[321] Just this year, a recent media campaign that took off was #trashtag, where users posted pictures of themselves cleaning up trash in local areas, while encouraging others to do the same.[322] So when it comes to exercise, apps such as MyFitnessPal or Fitbit could launch a campaign to encourage users to share their workouts with each other, or try to set a reasonable number of steps that individuals could aspire to reach each week. By sharing their progress online, users can encourage each other to become more active. It may also be a good idea for healthcare centers and government programs to work with advertising agencies to promote such campaigns. Michelle Obama's "Let's Move!" campaign is one example that can be used as a model for future movements.[323]

In addition, social media can be used in a more traditional way by simply allowing people to create groups and clubs based on their interests. For example, local officials may be able to create a Facebook group within the community for physical activity, such as ones for hosting touch football or ultimate Frisbee tournaments. This is something that is especially popular at colleges, with students organizing impromptu flag football or soccer teams to play in whenever they have free time.[324]

Closely tied to social media is the power of advertising as a tool to increase physical activity. One of the barriers we had previously cited was that many individuals simply aren't being made aware of the treatment options that are open to them. Most patients tend to ask for specific antidepressants when they see their physician, simply because they saw a commercial for one on television recently.[325] These commercials tend to be overly simplified, often using cartoon characters and flowery language to get their point across, which are appealing for individuals who just need a break from the symptoms and emotions they're experiencing.

Because this imagery and language is much more likely to stick, patients tend to bring only these options up with their physicians, which limits the scope of their discussion before it has even started.[326] But perhaps using advertisements can be helpful for other methods. It is of course much harder to utilize this method with therapy options, as these methods do not have large companies funding advertising campaigns on their behalf, and local counseling centers do not have the same reach that large drug companies do. But what about exercise? If we apply the same model here, we realize that large chains of fitness facilities and gyms do run ads nationally and globally. However, most of the focus tends to be on the physical benefits of exercise, often relying on attractive models to get their point across.[327] These commercials also have the added effect of targeting largely male audiences – although men and women buy gym memberships in equal numbers, twice as many women drop out within the first year as do men.[328] And out of those who do go to the gym, men tend to spend twice as much as time exercising as women do – gyms have struggled to provide adequate attention for the other half of the population.[329, 330]

I propose then that gyms start advertising the mental health benefits of exercise. By citing the studies that we have looked at, and by making a clear connection between exercise and its protective effects on our mental health, gyms and fitness products may be able to attract individuals who may not have previously been interested. Not only this, but it would give exercise greater visibility among the population, and perhaps would allow more patients to bring it up with their physicians as a potential way to deal with their symptoms. Additionally, the average working-class American would be better able to relate to the individuals in a well-constructed commercial than they would to actors and actresses, or bodybuilders and social media icons, who often promote fitness standards that are nearly impossible to achieve. And women, who suffer from higher rates of depression than other members of the population, may increasingly start to feel that the gym is not just a place for men, but a place where they can go to take care of themselves.

Below, I have created two simple advertisements that gyms could use to promote the idea of exercising for its mental benefits. Undoubtedly a skilled advertiser could capitalize on this idea to create much more effective media to reach the American population at large:

CONCLUSION

As I draw this thesis to a close, it is important to understand that there are countless other medical, legal, and social options that individuals and communities have to utilize physical activity to improve their health. Although I was not able to explore all of them in this paper, I encourage readers to explore new avenues to improve their mental health through physical exercise. While I hope that this thesis has helped to provide more information on how people can stay healthy, there were also many questions that I could not find answers for, or did not fit the scope of my work.

For example, I had initially set my sights on how patients and the public could integrate sleep, nutrition, and exercise to promote optimal mental health. I decided to focus on these three elements, because not only were they all crucial in helping me recover from my depression, these were three low-cost preventive measures that would allow people to exert more control over their lives. However, as I began writing my chapter on exercise, I realized that there was far too much information along these three routes for me to fit into a senior thesis, and that a more focused approach would suit this work better.

Even within the field of exercise, I was not able to delve as deeply into existing research as I wanted to. My ultimate goal was to promote the medicalization of exercise, and determine if I would be able to create guidelines for how to use exercise as a personalized prescription for each person, as well as each type of mental illness. Unfortunately, there just has not been enough research conducted at this point in time that is substantially more specific than what I was able to suggest in chapter 3.

Even within the field of research, there was a glaring disparity in the work done on male and female subjects – although women tend to be disproportionately affected by depression, most of the research into exercise more often tended to use male subjects, and did not give me much extra perspective into how exercise affected women. The field of exercise has traditionally been male-dominated, but I'd like to see that change in the future.

In my thesis, I also largely neglected looking at this issue from an economic lens – I've suggested quite a bit from a public health perspective, but I have not considered how these may positively or negatively affect the economy, or if some of these solutions are feasible from an economic standpoint. As I progress in my medical education and better understand our healthcare system, I hope to gain additional perspectives on how to effectively promote these solutions.

I also was prompted to think of the following after I was asked a great question by Dr. Kevorkian: "How many people who are already exercising are struggling with depression?" I was not able to find a concrete statistic regarding this fact, but I would hypothesize that this population fits under the subset of experimental subjects who found that their depression did not improve after exercising consistently. These subjects often tended to have much more severe symptoms, but many of them preferred therapy or antidepressants, which they may have simply responded better to. Much more research needs to be done in this area to formulate solutions when exercise doesn't seem to be working, even as a supplementary treatment. On top of this, I was not able to tie in a discussion about the idea of exercise perhaps even prompting depression in others – for example, bodybuilders have some of the highest rates of body dysmorphia out of all athletes and the general population. In this case, their desire to increase their muscle mass has

hurt their mental health, but this has not been the target of much research. As the movement on body positivity grows, this is a conversation that needs to be had – we already know that too much exercise is unhealthy physically – what about mentally? Moving on to the average Joe, many individuals feel uncomfortable stepping in the gym, or feel discouraged after a hard workout, and this may promote more negative thoughts about their self-worth and self-confidence. Lately women have been speaking up about "gymtimidation," stating that they stay away from the free weights area because they are afraid that the men in the gym may criticize them or overstep their personal boundaries. This type of behavior is unacceptable, especially when the gym is supposed to serve as a positive environment where people can improve themselves and take care of their health. These are issues that must be confronted head on, but I was not able to incorporate them into this thesis. It is my hope that I can address them in future works.

If you've read all this way, thank you for your patience and interest. I hope this was an informative read, and has left you with something you can use to improve your life, as well as the lives of those around you.

Thank you.

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BIOGRAPHY

Harideep Yeruva was born in Madras, India, on March 28th, 1996, and moved to Plano, Texas in 2006. He enrolled in the Plan II Honors program at the University of Texas at Austin in 2014, and double-majored in Neuroscience. He worked as a research assistant in Dr. Neal Rutledge's Ischemic Stroke Lab as a freshman and sophomore, worked as a Resident Assistant at Prather Dormitory as a sophomore and junior, and joined UT Rugby as a senior and fifth-year student. He was deeply involved in the Plan II Premedical Society, and volunteered at the New Century Hospice and Austin State Hospital throughout college. He will graduate in May 2019, also having earned minors in Spanish, Biology, and Psychology. After going through depression as a sophomore, he found exercise to be an invaluable tool in helping him recover as a junior and stay healthy as a senior and fifth-year student, and decided to focus his thesis on this topic. Harideep will intern at Congressman Lloyd Doggett's office in Washington, D.C., this summer to learn about public health policy, before starting graduate school at the University of Texas Rio Grande Valley School of Medicine.